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CONTENTS

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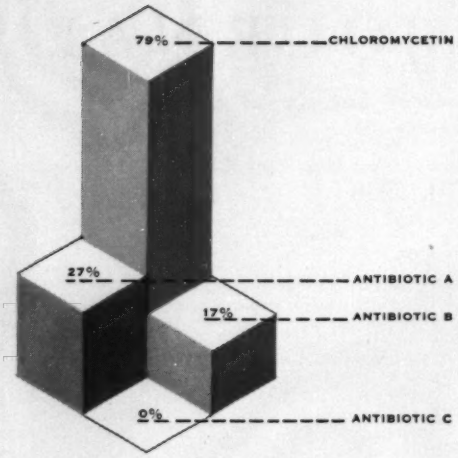
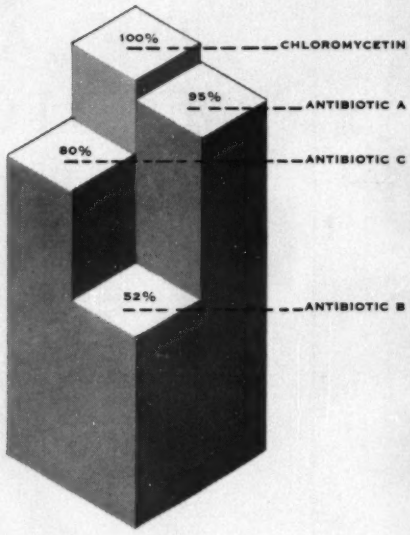
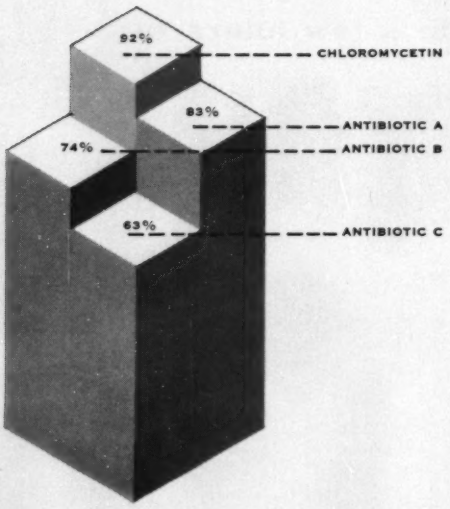
SENSITIVITY OF COMMON PATHOGENS TO CHLOROMYCETIN AND THREE OTHER MAJOR ANTIBIOTIC AGENTS*



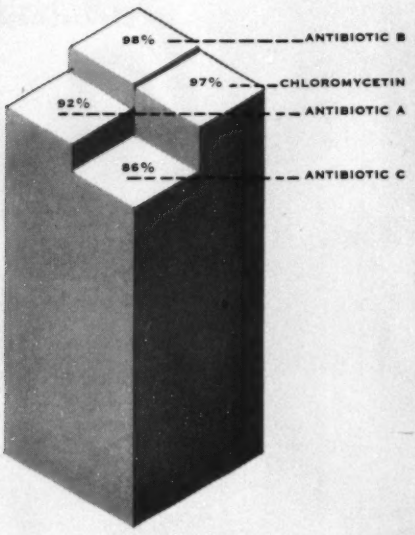
PROTEUS GROUP
(431-506 STRAINS)



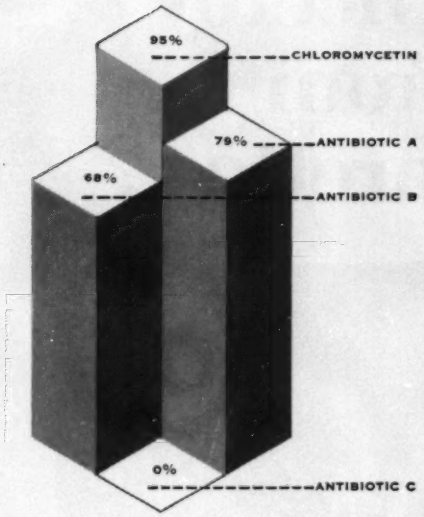
STREPTOCOCCUS VIRIDANS
(42-58 STRAINS)



NONHEMOLYTIC STREPTOCOCCUS
(109-141 STRAINS)



HEMOLYTIC STREPTOCOCCUS
(179-197 STRAINS)



AEROBACTER FECALIS
(14-21 STRAINS)

This graph is adapted from Altemeier, Culbertson, Sherman, Cole, Elstun, & Fultz.[1] It represents the second and concluding part of data presented in a previous issue.

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references: (1) Altemeier, W. A.; Culbertson, W. R.; Sherman, R.; Cole, W.; Elstun, W., & Fultz, C. T.: *J.A.M.A.* 157:305, 1955. (2) Weil, A. J., & Stempel, B.: *Antibiotic Med.* 1:319, 1955. (3) Jones, C. P.; Carter, B.; Thomas, W. L., & Creadick, R. N.: *Obst. & Gynec.* 5:365, 1955. (4) Austrian, R.: *New York J. Med.* 55:2475, 1955. (5) Murphy, F. D., & Waisbren, B. A., in Murphy, F. D.: Medical Emergencies: Diagnosis and Treatment, ed. 3, Philadelphia, F. A. Davis Company, 1955, P. 557. (6) Felshin, G.: *J. Am. M. Women's A.* 10:51, 1955. (7) Kass, E. H.: *Am. J. Med.* 18:764, 1955. (8) Tebrock, H. E., & Young, W. N.: *New York J. Med.* 55:1159, 1955. (9) Stein, M. H., & Gechman, E.: *New England J. Med.* 252:906, 1955. (10) Branch, A.; Starkey, D. H.; Rodgers, K. C., & Power, E. E., in Welch, H., & Marti-Ibáñez, F.: Antibiotics Annual, 1954-1955, New York, Medical Encyclopedia, Inc., 1955, p. 1125. (11) Munroe, D. S., & Cockcroft, W. H.: *Canad. M. A. J.* 72:586, 1955. (12) Norris, J. C.: *M. Times* 83:253, 1955.

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References: 1. Bunim, J. J., et al.: J.A.M.A. 157:311, 1955. 2. Forsham, P. H., et al.: Paper presented at First Internat. Conf. on Prednisone and Prednisolone, New York, May 31-June 1, 1955. 3. Perlman, P. L., and Tolksdorf, S.: Scientific Exhibit presented at A.M.A. Annual Meet., Atlantic City, June 6-11, 1955.

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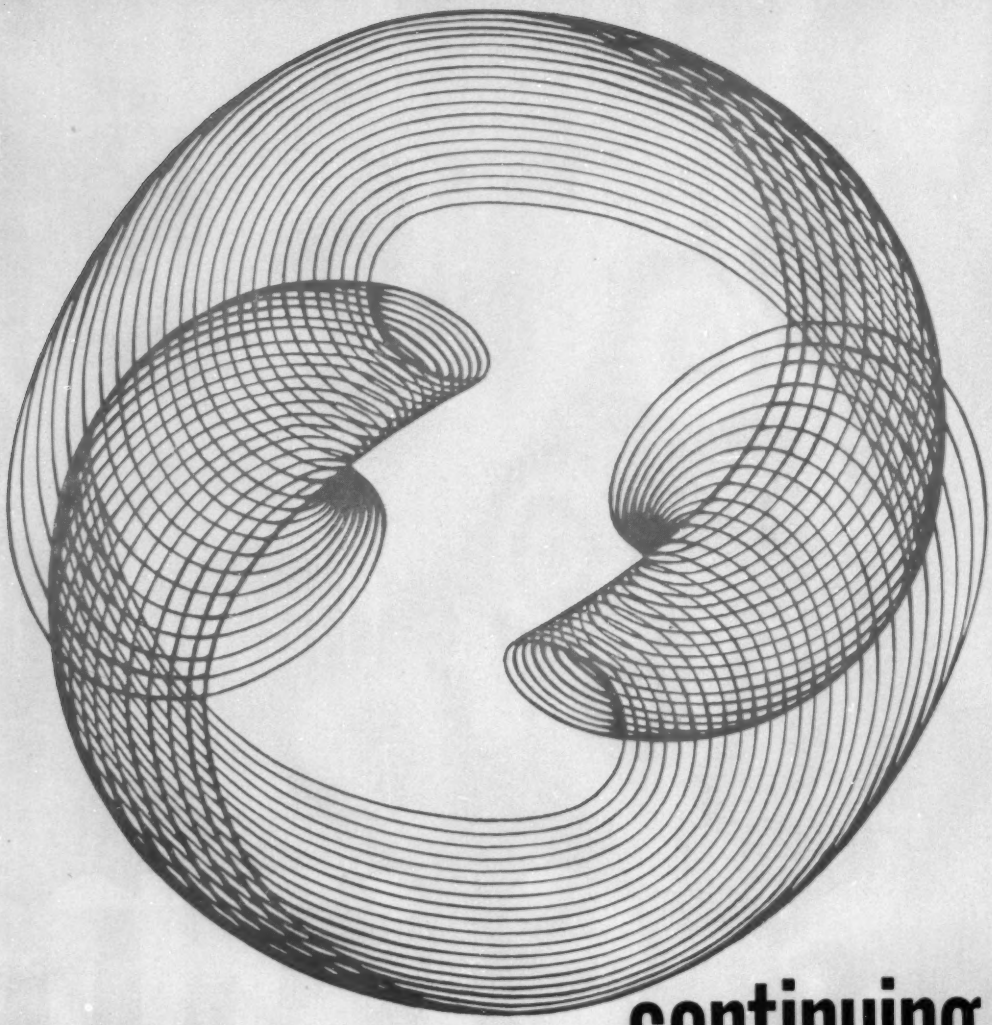

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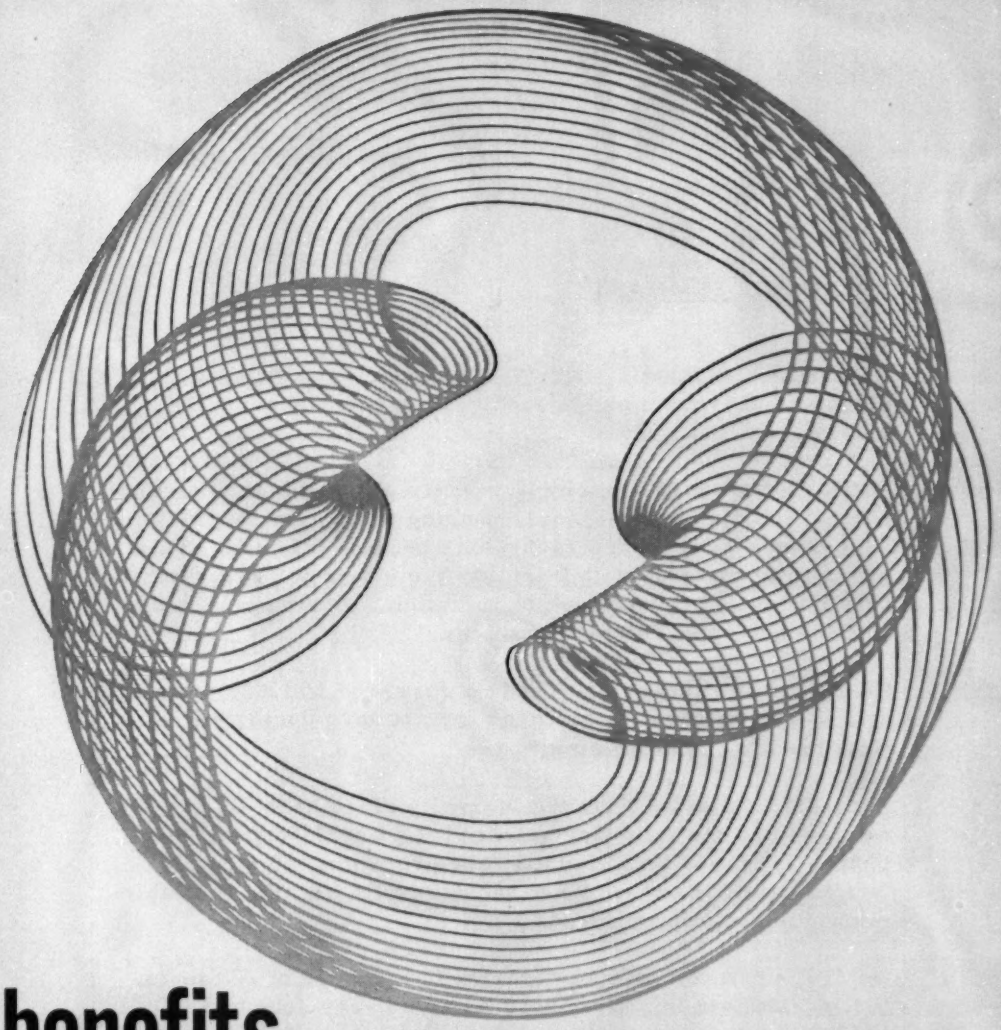

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Erythromycin in treatment of pyoderma*

8/12/55

DISCHARGE SUMMARY

Patient, white female, age 39, entered hospital with a diagnosis of lymphoma, proved to be lymphosarcoma by biopsy.

Initially she was treated by X-ray radiation, adrenal cortical hormone and an antinauseant. During this regimen she developed a generalized rash which became infected. This was a drug reaction with infection due either to (1) scratching or (2) a low WBC count due to radiation. A number of boil-like lesions appeared over the body.

On 8/4 penicillin was started in a dosage of 600,000 units daily. Penicillin was continued for six days during which time the pyoderma became worse.

Aspirated material from the lesions yielded hem. S. aureus, coag. + and the following sensitivities were obtained: penicillin, more than 10 units; erythromycin, 10 mcg.; tetracycline, 50 mcg. When these results became available penicillin was discontinued.

On 8/9, erythromycin was started in a dosage of 200 mgm. q.i.d. Marked improvement was noted very soon and by 8/12 almost complete healing of all lesions had occurred. Patient was afebrile throughout.

Final Diagnosis: (1) lymphosarcoma (2) secondary pyoderma due to hemolytic Staphylococcus aureus.

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*Communication to Abbott Laboratories

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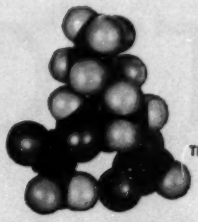

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Two articles in the April 30th issue of The Journal of the AMA[1,2] report on . . .

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1. Selling, L. S.: J.A.M.A. 157: 1594, 1955. 2. Borrus, J. C.: J.A.M.A. 157: 1596, 1955.

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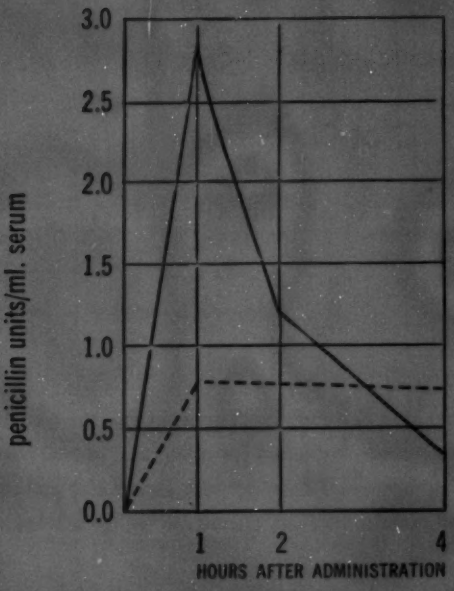

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1. Wright, W.W.: Personal communication.
2. Price, A.H.: Personal communication.

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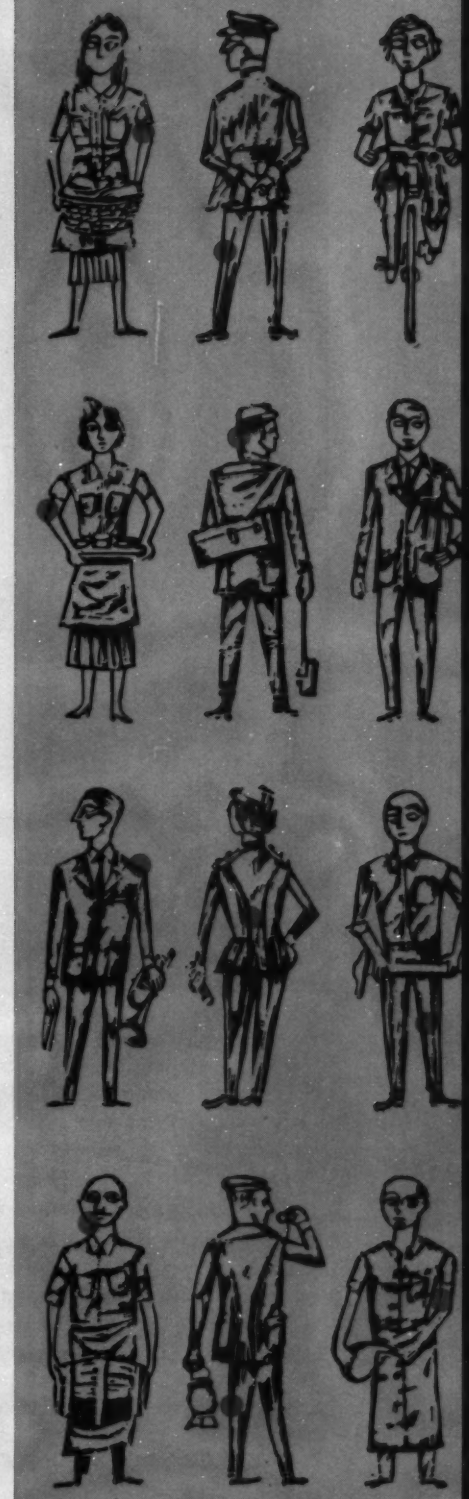

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VITAMINS AND OTHER NUTRITION FACTORS IN CLINICAL PRACTICE*

A Panel Discussion

Moderator—Lewis B. Flinn, M.D.,
Wilmington, Del.
Associate Professor of Medicine, Hahnemann Medical College; President, Medical Society of Delaware.

Robert S. Goodhart, M.D.,
New York, N. Y.
Scientific Director, National Vitamin Foundation.

Robert Kaye, M.D.,
Philadelphia, Pa.
Assistant Professor of Pediatrics, University of Pennsylvania.

Julius A. Mackie, M.D.,
Philadelphia, Pa.
Assistant Professor of Surgery, University of Pennsylvania.

Robert G. Ravdin, M.D.,
Philadelphia, Pa.
Assistant Professor of Surgery, University of Pennsylvania.

Dr. Goodhart: I understood that this was to be a panel and, since the most important part of a panel discussion is the question and answer period, I shall be as brief as possible in my introduction, and will not attempt to cover the whole field.

Some General Rules for the Use of Vitamins, and Other Nutrients in the Practice of Medicine

In order to set the stage for the evening discussion, I shall begin my remarks with a few categorical statements.

First: The various nutrients essential for life and health are effective only through the action of one upon another. There is no single vitamin, or other pure substance, that does not require other nutritional substances for activation, mediation and substrata.

Second: Except under experimental conditions, man rarely, if ever, develops a deficiency of one nutrient without an associated deficiency of others. Because of the unequal distribution of nutrients among foodstuffs, differences in requirements and differences in tissue susceptibility, it is the rule for the malnourished subject to demonstrate a predominance of the lesions of one or two deficiencies; however, it is not wise for the physician ever to assume that a single deficiency exists and to attempt therapy with a single nutrient.

Third: Poor diet (i.e., a diet markedly inadequate in certain nutrients, as judged by the Recommended Dietary Allowances[1] for presumably healthy persons) is only one of a number of causes of nutritional deficiency diseases, and rarely is it the sole cause in the United States, today. Other exciting and contributory causes include all those conditions that produce anorexia or otherwise restrict food intake; all those that increase metabolism and metabolic requirements, those that depress absorption from the gastro-intestinal tract or increase excretion, and those that interfere with the utilization of absorbed nutrients.

Fourth: Nutritional deficiency disorders may be acute, subacute or chronic, mild, moderate or severe, and various combinations of these circumstances may coexist. For example, it is common to find an acute, severe lesion on top of a mild chronic one. The recognition and identification of nutritional deficiency disorders requires the use of considerable diagnostic acumen by the examining physician. Incidentally, while the patient's dietary history is very important, his medical history is often more pertinent.

Fifth: In nutrition, as in any other branch of medicine, an ounce of prevention is worth a pound of cure. Nutritional disorders become increasingly resistant to therapy as they increase in chronicity and in severity. They are most susceptible to correction before anatomical lesions develop. Therefore, the importance of early diagnosis and treatment cannot be over-emphasized.

* Presented before the Medical Society of Delaware, Wilmington, October 17, 1955.

Sixth: The cardinal principles of nutrition therapy are:

(a) Begin treatment as early in the course of the disease as possible. Nutritional prophylaxis is the ideal.

(b) Use therapeutically effective amounts of the prescribed nutrients. The aim should be to build up the body's supplies to the optimum as rapidly as possible, and then to maintain them at this level, with a margin of safety.

(c) Provide all of the nutrients essential for life and health in sufficient quantities and in forms acceptable to and utilizable by the patient. Generally, it is desirable that the patient receive definitely therapeutic amounts of those nutrients the deficiencies of which are considered to be the cause of his symptoms, along with liberal amounts of all other necessary nutrients, with the exception that, in conditions other than caloric undernutrition, the caloric intake should meet but not exceed the caloric requirements. The proper treatment of obesity calls for a diet deficient only in calories and containing protective amounts of all other essential nutrients.

(d) Treatment should be continuous and prolonged. Remission of an acute lesion does not represent cure. Underlying chronic lesions and disabilities may remain, and relapses of acute lesions are common. Proper treatment involves the establismment of good nutritional hygiene in the patient, and the eradication of all contributory causes of malnutrition, or nutritionally compensating for them in so far as possible.

An interjection:-

The short time allotted me to introduce this evening's topic does not permit me to go into detail about specific nutrients; therefore, I am restricting my presentation to generalities, with the hope and expectation that it will stimulate questions from the floor that will enable this panel to resolve those particular problems of nutrition therapy with which you are most concerned.

To continue:-

A sharp distinction must be made between the prevention of nutritional deficiencies and the cure of existing nutritional deficiency states. The most efficient therapeutic amounts of the vitamins generally range from five to ten times maintenance amounts. However, there is considerable variability. In chronic vitamin A deficiency, daily doses of 100,000 to 150,000 I.U. of vitamin A may be necessary, while in vitamin C deficiency in the adult as little as 150 mg. of ascorbic acid daily may be curative. The intensity of treatment also will vary with the severity of the deficiency state exhibited by the patient and with the physician's estimate of the extent to which the patient's tissues are depleted. The water soluble vitamins, whether given by mouth or parenterally, always should be administered in divided doses throughout the day to prevent excessive waste by spillover into the urine.

A word about commercially available vitamin preparations probably is pertinent at this point. Pharmaceutical vitamin preparations are of two general types, supplemental and therapeutic. They may or may not include minerals, yeast and/or liver (as sources of unknown factors), and intrinsic factor to promote the absorption of vitamin B_{12}. Supplemental vitamin preparations are intended for the correction of dietary inadequacies and the prevention of nutritional deficiencies. They generally contain vitamin A, vitamin D, thiamine, riboflavin, niacin and ascorbic acid in amounts equal to or representing a substantial fraction of the Recommended Daily Dietary Allowances, when used as suggested by the manufacturer. They generally contain also forms of vitamin B_6, folic acid, pantothenic acid and vitamin B_{12}.

Although it is becoming more and more the practice for physicians to recommend multiple vitamin preparations as supplements to the diets of infants and young children, preparations consisting only of vitamin A and D continue to be marketed and widely used for this purpose.

Supplemental vitamin preparations often are suitable for the treatment of deficiency states in infants and young children but they are not intended to be used to correct such states in older children and adults. For this purpose, therapeutic vitamin preparations, containing much larger quantities of the vitamins per recommended dose, are available. Vitamins intended for therapeutic purposes are supplied in various combinations and singly to permit the most efficient use by the physician in the management of deficiency states which may be primarily of dietary origin or secondary to other disease states or metabolic aberrations. Therapeutic polyvitamin preparations are indicated for the correction of tissue deficits resulting from dietary inadequacy, even though functional or anatomic evidences of vitamin deficiency may not be demonstrable. This is in contradistinction to the use of supplemental vitamins for the prevention of dietary inadequacy.

The protein needs for depleted tissues are considerably greater than those for maintenance; however data are still meager regarding the quantitative needs for effective tissue repletion. Generally, amounts of protein ranging from two to three times the Recommended Dietary Allowances have been found to be effective as well as practical. 125 grams daily might well be regarded as the minimal therapeutic dose in the adult, to be attained as early as possible in the course of any disease or condition associated with increased protein catabolism. Unless muscle tissue is so considered, the body has no protein reserves and, under pathologic conditions, the loss of protein may be large, up to several hundred grams a day.

At least eight amino acids (lysine, tryptophane, phenylalanine, leucine, isoleucine, threonine, methionine and valine) are essential for man. In the absence of any one of these, all the others become useless for the purpose of tissue synthesis. The body apparently discards all essential amino acids not immediately utilizable and waits for the simultaneous delivery of a complete assortment before starting the synthesizing process[2]. Obviously, then, the nutritional value of any protein or combination of proteins is determined largely by its content of essential amino acids. Its ability to promote tissue synthesis is limited by that essential amino acid available to the body in smallest amount relative to need.

For the efficient utilization of dietary protein for body building, the protein consumed at each meal period should be complete, i.e., contain all of the essential amino acids in optimal amounts. Practically, this means simply that the physician should see to it that his patient receives a fair amount of protein of animal origin at every meal.

When sufficient amounts of high quality protein cannot be ingested in the form of customary foods, there is available a variety of protein concentrates such as egg white, powdered whole egg, casein, and hydrolyzed proteins. The physician should ascertain that the amino acid composition of the hydrolyzed protein of his choice is adequate and that at least 50 percent of it consists of single amino acids. The adequacy of a hydrolyzed protein can be determined by the ability of the preparation to support normal growth in immature rats or to produce weight gain in protein-depleted adult rats when fed as the sole source of protein[3,4,5].

Tissue proteins cannot be formed unless energy is available. With the available energy from fat and carbohydrate below a maintenance level, some protein must be utilized as a source of energy, thus diminishing the amino acids available for tissue synthesis. With adequate calories from other sources, the degree of protein utilization for tissue synthesis is proportional to the protein intake. An increase in the caloric intake above the critical level, however, does not result in any increase in the utilization of protein. All that results is a deposition of fat. The critical caloric level for the physically inactive, afebrile man appears to be about 1500-1800 calories per day[6]. In addition to adequate protein and calories, adequate amounts of the vitamins, particularly those of the B complex, are necessary for tissue synthesis.

The ratio of one nutrient to another in the diet is not a thing of prime importance. The important thing is that there be enough

of each and every one of the necessary nutrients. The calcium/phosphorus ratio in the diet assumes importance only when the content of either one of them is minimal. When the content of each of them is one gram or more, the quantitative relationship one bears to the other is of no consequence[7]. Nutritionally effective amounts of one nutrient do not cause the development of deficiencies in another, provided that all are present in amounts sufficient to meet metabolic requirements.

Whenever it is possible for the patient to ingest and assimilate sufficient nutrients, the oral route of administration is the route of choice. If it becomes necessary to give vitamins parenterally, intramuscular injection should receive first consideration. If the intravenous route seems to be the only practical method, the vitamins should be given in divided doses throughout the day or should be incorporated in slow infusions. The rapid intravenous injection of the water soluble vitamins is accompanied by considerable waste due to spillover into the urine. Intrathecal administration is rarely necessary.

The enteral administration of protein (by mouth, stomach tube or jejunostomy) is much to be preferred over the intravenous route, the only feasible parenteral route, as it is difficult to administer intravenously, sufficient protein and calories to effect tissue repletion without simultaneously administering an excess of fluid. In addition, all parenteral injections are expensive, unpleasant and not without danger. There is a place in medicine, however, for intravenous protein feedings and their use, when indicated, constitutes a great improvement in the care of patients.

Parental sources of protein may consist of whole blood or plasma or amino acid mixtures such as hydrolyzed proteins. In general, whole blood is indicated when there has been an external loss of blood or in inflammatory infections or other conditions where there is a hemoglobin deficit. Therapy with plasma is desirable where there has been a loss of plasma with resultant hemoconcentration, as in burns, intestinal obstruction and peritonitis and extensive extravasation from wounds.

In contrast to their value for the replacement of blood losses or for the correction of anemia, whole blood and plasma as sources of parenteral protein food are both expensive and unphysiological. The injection into the blood stream of an appropriate mixture of amino acids is a physiological method of alimentation. This is how ingested protein reaches the tissues. Injected amino acid mixtures supply to the tissues the building stones of protein and thus help to prevent tissue depletion.

I have scarcely more than touched upon problems of protein and vitamin nutrition and have said nothing about water, minerals, fatty acids, hormonal control, and other aspects of nutrition in clinical practice. No doubt the other members of our panel will discuss some of these. I have tried to summarize a few general principles, and I think that you will find the rules of nutrition therapy that I have set forth to be generally applicable and useful.

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President Flinn: Thank you so much, Dr. Goodhart.

I shall pass around some pieces of paper so if anybody's inspired they can write down their questions before we get into other aspects of this problem.

Next we will call upon Dr. Kaye to outline his aspects of the case.

Dr. Kaye read his prepared report, as follows:

VITAMINS AND OTHER NUTRITION FACTORS IN CLINICAL PRACTICE

Our group at the Children's Hospital of Philadelphia has been engaged in studies of protein metabolism in infants and in the use of fructose and fat in parenteral alimentation. I have successfully resisted the strong

temptation to report these studies to you tonight feeling that a broader selection of topics of nutritional interest might offer a more generally useful contribution to this symposium.

Recent work by Dutch[1] and English workers[2] has implicated gastro-intestinal sensitivity to wheat and rye gluten as important etiologic factors in the celiac syndrome. Almost all patients have responded well to the administration of diets from which these substances have been eliminated. The first slide illustrates the dietary items which are well tolerated by the patients. [Slide 1. — Celiac Diet. All meats and fish — whole milk — fruits — vegetables — potatoes — rice and oats — butter and cheese — other fats — eggs — sugars.]

This liberal diet, supplemented with vitamins, is nutritionally adequate and eliminates the occurrence of deficiencies of calories and protein which were formerly encountered in severely affected patients.

Pancreatic fibrosis has been recognized with increased frequency in recent years. The respiratory complications are so prevalent that excluding asthma, it is by far the chief cause of chronic pulmonary disease in children in this area. It is frequently confused with whooping cough or bronchiectasis. Its presence should be suspected in children who show evidence of greatly prolonged or recurrent infection of the lower respiratory tract whether or not there is accompanying evidence of bulky stools, wasting or excessive appetite.

Recognition of this disease has been simplified by the almost uniform demonstration of an excessively high concentration of sodium, chloride and potassium in the sweat of patients with this disease[3]. The upper limit of normal concentration of these electrolytes in sweat is approximately two-thirds of their serum concentration namely 100 and 65 mEq/liter for sodium and chloride respectively. The "sweat test" serves also to detect those patients with fibrocystic disease who have normal or partial pancreatic function.

While the prognosis of this disease remains grave, therapy with potent enzyme preparations such as Viokase and administration of broad-spectrum antibiotics offers much toward maintaining a fairly satisfactory nutritional and respiratory status in these patients.

An often life-saving advance in parenteral nutrition has come about through an increased awareness of the frequency and clinical significance of deficits of the intracellular cation, potassium. These have been classified by Cooke[4] into categories of inadequate intake, excessive losses, and redistribution of potassium ion. Inadequate intake is most frequently caused by starvation and prolonged parenteral treatment with saline and glucose. Excessive losses occur in the gastrointestinal disorders of diarrhea, vomiting and as a result of prolonged suction. Urinary losses may occur in intrinsic renal disease, especially chronic nephritis and lower nephron nephrosis, in the recovery phase. A similar result may be brought about by the action of extrinsic influences on the kidney such as alkalosis, diabetic acidosis and mercurial diuretics. Hyperadrenalism may also lead to potassium deficiency either endogenously as in Cushing's disease and stress or exogenously as the result of treatment with ACTH, cortisone or Doca. Redistribution of potassium from the extracellular to the intracellular phase in treatment of diabetic ketosis and familial periodic paralysis may also lead to clinically significant potassium deficiency.

Potassium ion, which is the chief intracellular electrolyte, plays a vital role in the functioning of many organs, tissues, glands and metabolic reactions. The most striking evidence of its deficiency are weakness of skeletal muscle, smooth muscle atony often leading to intestinal ileus and cardiac muscle dysfunction. The latter may result in increased pulse and venous pressure and cardiac failure. The electrocardiogram may be helpful in recognizing potassium deficiency as it characteristically shows prolongation of the Q-T interval and decreased amplitude of T waves.

Potassium deficiency may be treated by parenteral administration of potassium in a dosage of 3 mEq/kg. or (100 mgm. KCI/lb.) This quantity should be administered over a period of 4-6 hours and only after urine flow has been well established by prior treatment with sodium chloride, glucose

and water. These precautions should be observed to avoid the dangers of toxic accumulations of potassium. It is desirable to provide this quantity of potassium to all infants and children who are maintained on parenteral feedings as well as to those with deficits.

Fatalities in infants with diarrheal dehydration are fortunately uncommon. Those which do occur are almost entirely limited to the initial hours and the period after the first week of treatment. The early fatalities are the result of shock and toxemia and the late deaths to starvation. Starvation may be largely the result of prolonged under-feeding, prescribed because of the continued passage of diarrheal stools. Holt and Chung have demonstrated the presence of significant retentions of the protein, fat and minerals of oral feedings in diarrheal infants. For this reason, the only indications for withholding oral feedings beyond the first day or two of treatment are debility of such a degree as to constitute a real threat of aspiration, the occurrence of severe vomiting and the development of marked abdominal distention.

Recent work by Bickel[5] and by Armstrong and Tyler[6] has led to the hope that the severe mental retardation of patients with phenylpyruvic oligophrenia may be ameliorated by dietary means. Patients with this condition constitute approximately 1-5% of the institutionalized mental defectives in this country. About 80% of the affected individuals are blonde and blue-eyed. The condition is easily diagnosed by detection of phenylpyruvic acid in the urine. The test consists simply of adding 5-10 drops of 10% ferric chloride solution to 5 ml. of urine. The development of a dark blue-green color constitutes a positive reaction.

The biochemical defect consists of a failure to oxidize phenylalanine to tyrosine and considerable improvement in mental capacity may follow the reduction of phenylalanine in the diet. Because of the presence of approximately 5% of phenylalanine in all dietary proteins, special mixtures which are now commercially available are required.*

* Allen & Hanburys Co. Ltd., Bartor Road, Toronto 15, Ontario, Canada.

Perhaps the greatest benefit from this regime may be its application to affected young infants who are most likely to be discovered in families in which an older sibling is known to be affected with this disease.

Galactosemia is an infrequent condition but not so rare as the small number of recorded cases might suggest. Its recognition in early life is important because a simple means is at hand for prevention of the growth failure, hepatic cirrhosis, cataracts and mental retardation which occur in the untreated patient. The clinical manifestations are sufficiently characteristic as to make diagnosis relatively easy if the possibility of its occurrence is considered. The combination in an infant of poor weight gain, diarrhea and vomiting, marked hepato and splenomegaly with the finding of a positive reaction in the routine test for urinary sugar makes the diagnosis highly probable. Definite diagnosis is made by failure of the urinary sugar to be fermented by yeast and its identification as galactose by chromatographic means or by the formation of its characteristic osazone with phenylhydrazine. Other common manifestations are jaundice and lamellar cataracts as illustrated in the slide.

The metabolic defect in these patients lies in an inability to convert galactose to glucose. The pathologic manifestations are related to accumulation of galactose. Early elimination from the diet of galactose, which is derived from the lactose of milk, brings about reversal of the pathologic features of the disease. This is readily accomplished by substituting the lactose-free milks, Nutramigen or soy-bean milks, for human or cow's milk.

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Dr. Mackie: Dr. Ravdin asked me to address to you his regrets in not being able to be here tonight due to rather sudden and unexpected illness. He prepared this paper and I shall try to present it and I beg your forgiveness for any unfamiliarities I might come up with in this presentation.

(Dr. Mackie read **Dr. Ravdin's** prepared report, as follows):

THE ROLE OF VITAMINS IN SURGERY

The nutrition of surgical patients can be categorized conveniently under three headings: nutrition in the acute phase of disease or injury, including the trauma inflicted by operative procedure; nutrition in the convalescent phase; the use nutriments for special purposes in particular circumstances. It is convenient also to discuss vitamin administration under these headings, with the tacit understanding that vitamins integrate with the general nutritional program and their consideration as a separate entity may prove very difficult to justify.

Let us look then first at what we may call the acute phase: the disease state as it presents to the surgeon, and the effects of the surgical procedure itself. Here we are concerned with two problems, the correction of such deficits as may exist originally, and maintenance while the patient weathers the storm, attains even footing, and begins the upward course. As a rule, this is a short term problem, one we can think of in dimensions of a couple of weeks at most, often days, and for this reason the fat soluble vitamins do not commonly enter our deliberations. The water soluble vitamins, on the other hand, in particular the B group and ascorbic acid, have a more rapid turnover rate and no known storage mechanism as such, and it is entirely reasonable to suppose that they should be supplied for maintenance purposes. Actually, agreement with this principle is such a wide spread practice in American surgery, particularly in conjunction with parenteral fluids in the immediate postoperative period, that it is difficult to assess the importance of vitamins from clinical data. From time to time reports appear in the European literature of full blown deficiency pictures following major surgical procedures. This coincides with experimental experience. It has, in fact, been standard practice for years to precipitate deficiency states by challenging the animal with some sort of stress which we may think of as corresponding with the stress of acute illness and operation. The question, therefore, is not whether to supply the water soluble vitamins; we are all in agreement as to their desirability. It is rather a question of how much?

Out of a welter of speculation, a few fairly secure observations emerge to guide us. Stress alone cannot produce a deficiency state in a well-nourished individual, animal or human. In fact, a rigorous program of deprivation is necessary, a good deal more rigorous than can be expected in the bulk of clinical material we encounter. We may note that a proportion of our patients come to us with demonstrably *less than* optimal vitamin levels. This applies, of course, to patients with wasting diseases, such as malignancy, tuberculosis, or ulcerative colitis, but also to patients treated over significant periods with broad spectrum antibiotics, whose intestinal flora may no longer contribute to their vitamin intake, and to patients with hyperthyroidism, whose metabolic activity may out pace their supply and produce a relative inanition. On the other hand, "*less than optimal*" has a very much more distinct *chemical* meaning than a *clinical* one. There is a very broad range of "less than optimal" determinations which are entirely compatible with clinical well-being: it is, in fact, difficult to correlate a given set of values with the clinical state until in the very lowest range, the *deficiency picture* is present.

To illustrate more concretely, we may look at some of the observations on ascorbic acid. Although more is known of the various B-vitamins in intermediary metabolism, and they appear more intimately related to the essential enzymatic processes, vitamin C has always been of interest to the surgeon because of its direct influence on the strength of wounds. Save for hypoproteinemia, scorbutus is the only deficiency state known to interfere with wound healing. Here again, however, the evidence is clear: short of frank scurvy, wound strength is not interfered with. At least, there are no gradations

in strength corresponding to various "suboptimal levels". The data indicating that an individual can not be kept saturated with ascorbic acid unless huge doses are given, suggesting enormous deficits, must be examined in the light of the British studies, done during the war when vitamin C sources had almost vanished from the diet. These showed that plasma levels of ascorbic acid could dwindle to the vanishing point without scurvy, and that intake of quantities of a fifth of the recommended daily requirement produced no *clinical* changes, although *chemical* changes were readily found. Essentially no intake at all could be tolerated for months, but very minor stress would then promptly produce scurvy.

We can conclude, then, that during what we are calling the acute phase in handling surgical patients, provision of the B vitamins and ascorbic acid in quantities of the order of two or three times the minimal daily requirement will prove entirely satisfactory, and allow for at least a moderate degree of "suboptimal" nutrition before the patient comes under treatment.

The importance of nutrition in the convalescent phase is obvious enough to bear little comment. The patient has further wound healing to accomplish, his preoperative weight, strength, and energy to regain, and frequently blood volume to make up by hemoglobin and plasma protein synthesis. During this anabolic period sufficient vitamins must be supplied, and may be added to the diet if this is not adequate, as well as employed to stimulate the appetite. Certain situations, however, require more than casual attention to convalescent nutrition. For example, in extensive burns nutrition may well make the difference between success or failure for a patient whose initial resuscitation has been safely accomplished. All nutriments, including vitamins, must be pushed vigorously and constantly in amounts four or five times the usual requirement, because of the great drain produced by large open areas. A rather comparable situation obtains in patients having undergone total gastrectomies, or extensive resection of the small bowel, where inefficient absorption may increase the nutritional requirement. A certain proportion of totally gastrectomized individuals, and some with extensive subtotal resections, will develop a macrocytic anemia which responds to vitamin B_{12}, though this is a late finding, well outside what is usually considered the convalescent period.

This brings us, then, to the consideration of special uses for vitamins in surgical conditions. With the exception of vitamin B_{12} mentioned before, these are particularly concerned with fat soluble vitamins. Let us pass over the tocopherols very briefly, to say that vitamin E has not proven of any significant help in the management of cicatricial conditions such as Dupuytren's Contracture, nor has it shown consistent antithrombin activity to justify its use in the prophylaxis of thrombophlebitis. Vitamin D, however, has an important role in the treatment of postoperative hypoparathyroidism. This condition may be anticipated in about 2% of patients following extensive subtotal thyroidectomy, and is usually relatively transitory. It attends the removal of functioning parathyroid adenomas with a much higher relative frequency; here the tendency to tetany may be aggravated by the withdrawal of calcium from the serum into so-called "hungry bone". Substances with vitamin D activity ameliorate this situation by facilitating calcium absorption from the gut, and by inhibiting phosphate reabsorption from the renal tubule. The latter effect corresponds with Albright's concept of the action of parathormone, and for this reason he proposed AT-10 as the agent of choice; this tachysterol exerts its influence more on the kidney than on the gut. The additional expense involved, however, is not justified clinically, and the more readily obtained ergosterols are perfectly suitable if given in large enough doses, along with liberal amounts of calcium and restricted phosphate. It is important to re-evaluate the state of calcium and phosphorus metabolism periodically, because parathyroid function has a tendency to recover, and vitamin D is the only vitamin whose overdosage is clinically detrimental.

Naphthaquinones with vitamin K activity have also been of great surgical interest

ever since the discovery that their failure to be absorbed by patients with obstructive jaundice led to the bleeding tendency which had plagued surgeons for decades. Parenteral or oral administration of the sulfite or phosphate esters of methyl naphthaquinone has solved this problem, allowing the liver to resume the synthesis of prothrombin and to correct the coagulation mechanism. These substances, Hykinone or Synkavite, are not nearly so reliable in restoring the prothrombin level following the administration of Dicumarol, phenylindandione, and related compounds. Since these anticoagulants are often used in surgical practice in connection with thrombophlebitis, and because patients anticoagulated for various reasons must come to operation, the natural vitamins K, K_1 or K_1 oxide, have been valuable additions to the aimamentarium. It has been shown repeatedly that doses of these emulsions in the range of 50 milligrams will produce a definite increase in prothrombin within four hours, and a safe level within eight hours in almost all cases, whether given by vein or by mouth. The K_1 emulsions will also work in some instances in liver damage when the water soluble preparations will not; they should be given repeatedly over several days before deciding that they have failed.

President Flinn: Before we get into the discussing of the questions, Dr. Goodhart you're doubling for Dr. Tompkins. Are vitamins of any use in obstetrical practice?

Dr. Goodhart: As I indicated in my paper and as the other speakers have brought out, stress situations, no matter what they may be, are apt to precipitate nutritional deficiencies. Pregnancy is a stress situation.

Dr. Tompkins divided his pre-natal patients into groups, at random. One group received an ordinary diet and the best prenatal care possible at his hospital. A second group received the same pre-natal treatment plus a multiple vitamin capsule. The third group received the same pre-natal treatment, plus vitamins and supplementary protein, in the form of casein. There also was a group that received the supplementary protein without the vitamins. The group that did the best was the group that received the protein plus the vitamins. The group that received the vitamins alone and the group that received the proteins alone did not do so remarkably well, although in some respects they did better than the control group. This was not unexpected.

Vitamins work as accessory food substances or activators. They do not furnish any substrata for energy production or tissue construction. They make it possible for the body to use carbohydrates, fat and protein. Given sufficient energy, protein may become the limiting factor in the presence of an adequate quantity of vitamins. When you give the vitamins plus protein, and have sufficient calories, then you don't have any limiting factors and the patients do well. This is precisely what Dr. Tompkins found. He found some other things of interest; for example, obese women who become pregnant do not do so well. But they do less well if you attempt to reduce them during pregnancy. Patients who are underweight don't do so well either. They do better if they are fed properly and gain weight during pregnancy.

There has been some argument among obstetricians in and around Philadelphia about Dr. Tompkins' findings on the obese women, but I think that the results are definite. They are statistically significant. Obese pregnant women placed on reducing diets do very poorly. The way to treat such a mal-nourished woman is to treat her before she becomes pregnant and not after she becomes pregnant.

Dr. Tompkins found that the obese women had a very high incidence of toxicities and that the undernourished, the thin women, had a high incidence of premature deliveries.

When the woman was fed properly, given sufficient calories to permit growth of the baby and given an adequate amount of protein and vitamins, she did not get a bigger baby. Many women erroneously believe that if they get enough to eat they're going to get a huge baby. Obese women have large babies, but, the obese women in Tompkins' study, who were fed properly, had smaller babies than those obese women who were on the control diets.

I think that Dr. Tompkins has demonstrated that: First, giving only vitamins is

not enough. It is necessary to give also a substrate for the vitamins to work upon. And, secondly, if you want to do a really good job with pregnant women, you must start before they are pregnant.

President Flinn: Thank you so much. I have a few questions here with which we will start off and if anyone feels so inspired to ask others, he may do so.

What evidence is there, direct clinical evidence, that excessive amounts of B complex or individual members of B complex are not toxic to man?

Dr. Goodhart: I said in my paper that given a sufficient amount of all of the nutrients, an excess of any one nutrient is not toxic. By that I don't mean a great excess such as you get with great amounts of vitamin A, or huge amounts of vitamin D. The spread between the therapeutically effective amounts of the vitamins and toxic amounts is very great. I know of no evidence for toxicity of any of the B vitamins when orally administered.

There are some hematologists who say that folic acid is dangerous and should not be put in multiple vitamin pills, should not be sold freely to the public, or made generally available to the physician in multiple vitamin preparations, because folic acid promotes vitamin B_{12} deficiency and promotes combined system disease, while permitting the patient to maintain a normal blood picture, thus the Doctor may fail to recognize that the patient has pernicious anemia. What actually happens here? I had occasion to review what was going on prior to the availability of folic acid. About 25 per cent of all patients with pernicious anemia develop neurological signs before they develop any abnormal blood picture. Some don't develop any hyperchronic, macrocytic anemia at all. Eighty per cent of all pernicious anemia patients, inadequately treated or not treated, sooner or later develop some combined system disease. From reviewing the literature since folic acid, I conclude that the situation has not changed. The proportions remain about the same. That is, you still get about 25-30 per cent of the patients coming in with neurological signs and no marked abnormality in the hematological picture, and about 80 per cent of those who are carried on folic acid, alone, or are otherwise inadequately treated develop neurological signs.

President Flinn: Do multiple vitamin preparations which contain folic acid contain sufficient folic acid in those capsules to correct pernicious anemia?

Dr. Goodhart: As little as 1.0 mg of folic acid daily usually will induce a hematopoietic response in a patient with pernicious anemia in relapse. This amount, and more, can be readily obtained from a good diet; that is, a diet high in green-leafy vegetables and otherwise following what is accepted by our nutritionists as conforming to the best dietary practices. Most multiple vitamin capsules contain from 0.25 to 0.50 mgm of folic acid per capsule, if they contain any at all. Undoubtedly such levels of folic acid, added to that contained in the diet, can serve to maintain a normal blood picture for variable periods of time in some patients with pernicious anemia.

It must be borne in mind that the patient with pernicious anemia does have a requirement for folic acid. There are, on record, some cases, treated with vitamin B_{12}, which eventually developed hematological relapses that responded to folic acid.

Vegans, in England, who eat no animal food whatsoever, develop vitamin B_{12} deficiency and they, interestingly enough, develop the neurological signs without any abnormal blood picture. This is due to the fact that they have a high intake of green vegetables, particularly high in folic acid. So, taking the folic acid out of multiple vitamin capsules is not going to protect pernicious anemia patients, a certain number of them, from developing neurological signs prior to the characteristic blood picture. The physician must learn to recognize and diagnose vitamin B_{12} deficiency, the primary manifestation of which is a neurological disorder.

President Flinn: Is there any danger as far as leukemia is concerned?

Dr. Goodhart: Folic acid does not cause leukemia, and folic acid antagnosists have not proven to be the cure of leukemia. There is no more that we can say about the problem, at this time.

President Flinn: Dr. Kaye, do you give green vegetables to your children?

Dr. Kaye: If they'll take them.

President Flinn: I might ask Dr. Kaye this one. I can throw it around. Why are therapeutic doses of vitamins 5 to 10 times the maintenance need? Poor absorption, poor utilization, chemical mass action, reducing time of tissue repair, it didn't say here, or for business reasons?

Dr. Kaye: The patient who requires therapeutic doses has probably depleted those vitamin stores which the well-fed patient would have, so that one has not only the problem of maintenance requirement but the restoration of stores. Many of the patients who require therapeutic vitamin preparations, as has been said before, have increased metabolic requirements associated with fever, stress, or with hyperthyroidism. I think that there is no question in the treatment of rickets and scurvy, which are the nutritional diseases most commonly seen in pediatrics, that one can achieve a much more rapid response with dosages 5-10 times as great as are required to prevent the deficiencies in the first place.

President Flinn: Any argument about that?

Dr. Goodhart: No, I made a similar statement and I would say that my statement is on empirical grounds. In the early days when we tried to treat these things, we found that results were much better if you increased the dose, but, for most of the water soluble vitamins, amounts greater than five times the daily requirements in one dose proved to be wasted. There is not much point in going beyond that, so far as water soluble vitamins are concerned, because the spillage into the urine becomes very high. So that we settled upon five to ten times the daily requirement, until the patient approaches saturation, and then we try to maintain him at that level. Giving extremely large amounts at one time is generally a waste of money and vitamins.

President Flinn: Dr. Mackie, what are your recommendations for vitamin therapy in severe third degree burns?

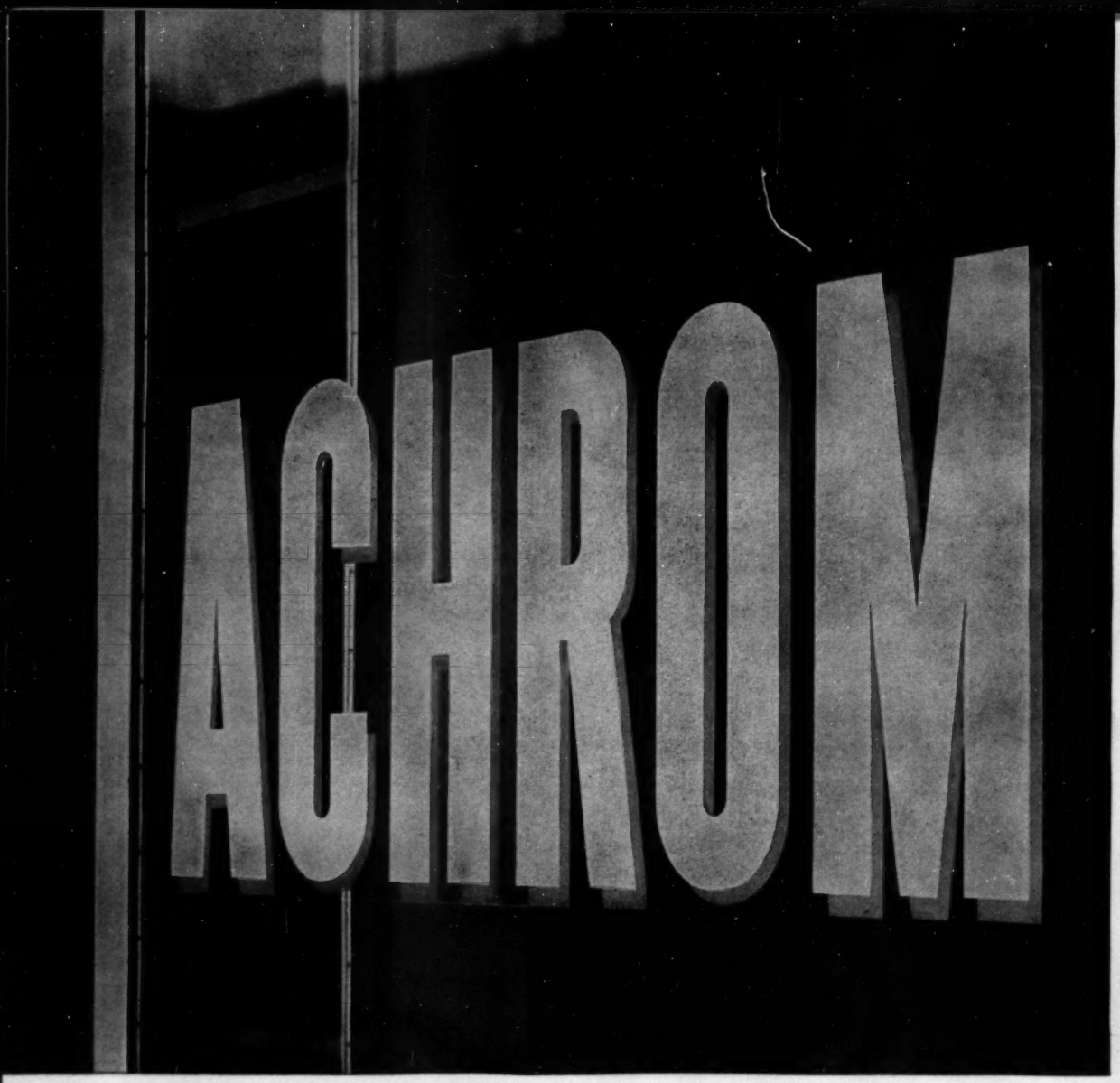
Dr. Mackie: Well, I would classify that, I suppose, along with more demanding conditions for supplementals, I shouldn't say supplementals, but additional vitamin therapy. Somewhere in the neighborhood of five times the normal daily requirements would be in the range of what we customarily give to a patient who has a severe burn, in his first week or ten days to two weeks.

President Flinn: Thank you.

Dr. Goodhart, man is perhaps the only animal to continue to drink milk beyond the period of childhood. Will you comment on this especially in respect to (1) normal adult requirement for calcium, and (2) possible relation to development of arteriosclerosis?

Dr. Goodhart: Well, I think what we have to bear in mind is that man has no requirement for any specific food. We require certain nutrients, we don't require milk, we don't require bread, we don't require meat. We require amino-acids, calories, certain fatty acids, certain vitamins, minerals, and waters. And how we get those things depends upon our dietary customs. We have a requirement for calcium, around 8/10 of a gram a day. But it is not required that we get this calcium through milk. The only other things of importance that milk provides are riboflavin and protein. Other good sources of high quality protein are available. Unfortunately, in our customary diets, without enrichment, it is extremely hard to meet the recommended allowances for riboflavin, without consuming some milk every day, or some milk products. The enrichment of flour, cereals and bread has been the answer to this problem for many people. For others, the use of pharmaceutical vitamin preparations has proven to be the answer.

Now so far as cholesterol is concerned this is a moot point. We know that the cholesterol level of the blood can be decreased by a fat free diet. It can be decreased by a diet which is entirely free of animal fats, but containing a liberal amount of vegetable fats. But what we don't know is whether or not the blood cholesterol level has anything to do with the genesis of arteriosclerosis or althero sclerosis. Dr. Reinhart of California and Dr. Emerson of the Merck Institute have been able to produce, in the monkey, a typical arteriosclerosis with a vitamin B_6 deficient diet which, in-



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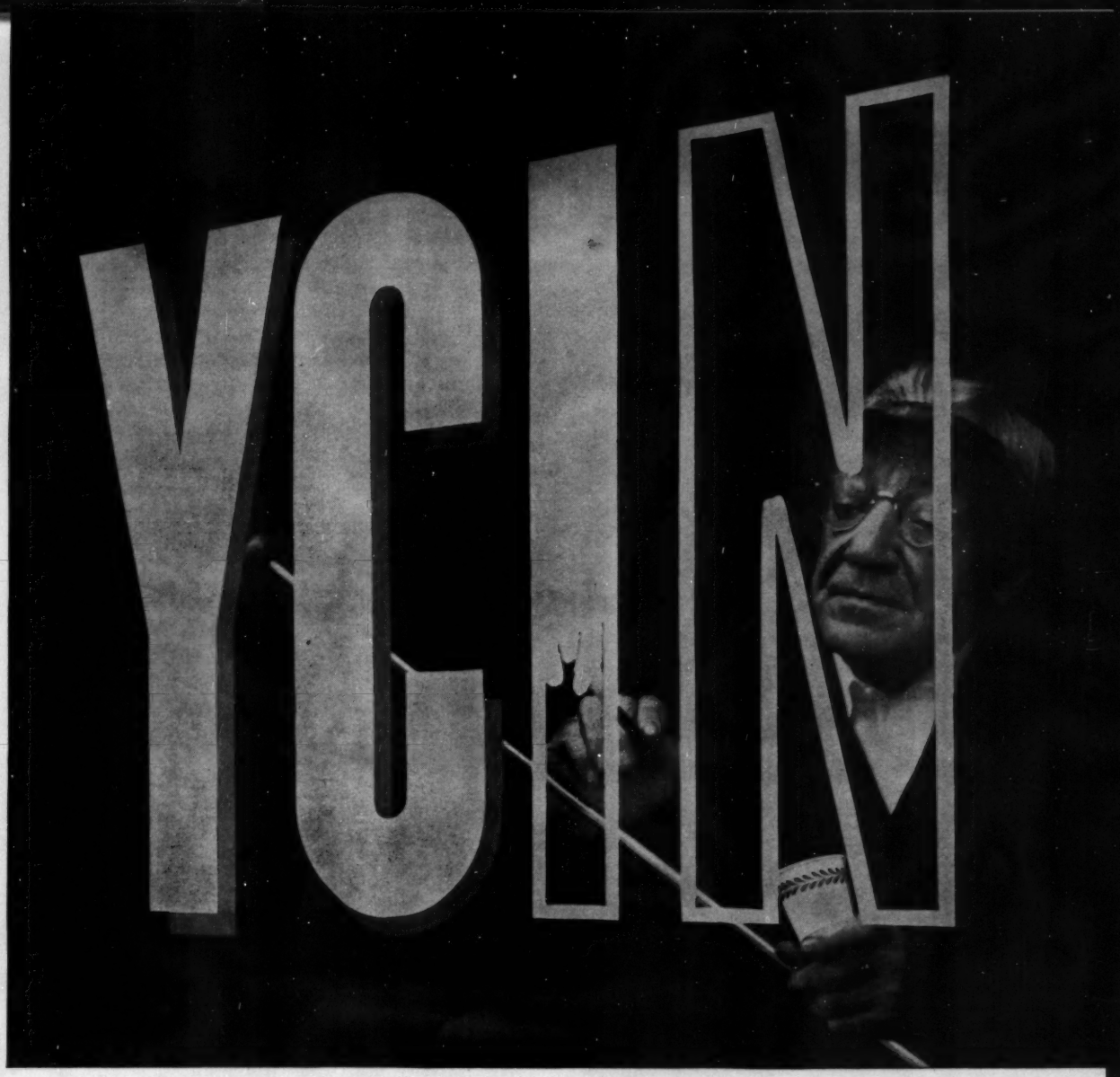

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cidentally, was very low in fat, and very low in cholesterol.

Another thing I might say a word about at this point is this. We must think a little bit of what we want from people. The things that build up a football player, or a chap that can produce healthy children, or a woman who can nurse her child are not necessarily the same things that prevent coronary heart disease or promote long life. Every laboratory doing nutritional studies on the rat has been able to demonstrate that on a high fat diet you can get a bigger rat, a healthier and stronger rat, a rat with more progeny, and a rat that can nurse its young and otherwise meets every criterion of good health, except that he doesn't live as long as the other rats.

President Flinn: Dr. Kaye, I'd like to ask you this one perhaps. A recent article in the Margaret Hague Bulletin seems to indicate a greater need for calcium than phosphorus during pregnancy. Will you comment on that, or refer that to Dr. Tompkins?

Dr. Goodhart: The National Research Council recommends that the phosphorus allowance should be at least equal to that for calcium during the latter part of pregnancy. The fact is that, if you have enough of each, you don't have to worry about the ratio of one to the other.

President Flinn: Do you agree with that?

Dr. Kaye: I wondered about that when you said that before. We sometimes use high calcium intakes to prevent the absorption of phosphorus in patients with renal insufficiency and phosphorus retention, on the assumption that one can sufficiently exceed the usual calcium intake and thereby interfere with the absorption of phosphorus. Do you agree with that?

Dr. Goodhart: Well, I suppose you can give enough calcium to prevent phosphorus absorption but I don't know that there is any nutritional range that would have any effect.

Dr. Kaye: I think you probably have to achieve that by using mineral supplements.

President Flinn: You're thinking more of an acute case, aren't you?

Dr. Kaye: No, phosphate retention is a clinical problem chiefly in the child with severe chronic renal insufficiency.

President Flinn: Well, why not use Ringer's solution, Dr. Kaye, routinely in the presence of normal kidney function when parenteral fluid is indicated to prevent and/or correct mineral deficiencies?

Dr. Kaye: This would be an improvement over saline and glucose, but in the presence of defects, Ringer's solution which has about ten milliequivalents of potassium per liter is probably inadequate to correct the deficit. It has been shown that the retained potassium is of the order of three or four milliequivalents per kilo per day and the kidney paradoxically will excrete potassium even in the presence of deficiency. So that intakes above the amounts provided by Ringer's solution would probably be necessary, although Ringer's solution would be an improvement over sodium chloride and glucose. It is rather interesting to know that the concentration of potassium in milk is approximately 4 milliequalents per 100 ml. which is about the same concentration as the 40 milliequivalents per liter present in Darrow's solution and about twice the concentration of potassium present in Butler's solution. The strength of the solutions which we use are the order of 20 to 40 millequivalents per liter. For those of you who like to think in milligrams, a milliequivalent of potassium is 40 milligrams.

President Flinn: Thank you.

How many days or weeks is storage of fat soluble vitamins in an average healthy adult sufficient protection against tissue damage in case of acute deprivation, assuming that the patient is on a 1500 calorie intake which is equal to the daily need.

Dr. Goodhart: The requirements for the fat soluble vitamins bear no relation to the caloric intake. An individual who is on a diet which is absolutely zero in vitamin A, assuming that he was well nourished with vitamin A before he started this diet, would not develop any signs of vitamin A deficiency for twelve to eighteen months, or longer. The speed of the thing would be stepped up by certain stress situations but how much I do not know. The vitamin of which man develops a deficiency the most rapidly, appears to be thiamin. Thiamin deficiency has been demonstrated within a period of four weeks.

President Flinn: How about toxic doses of thiamin? Is there such a thing? You have partially answered that, but suppose somebody gets a 100 milligrams a day of thiamin, is that more than is necessary parenterally?

Dr. Goodhart: 100 mgs of thiamin, parenterally is certainly more than is necessary but is not toxic. Experimentally, by adding high concentrations of thiamin directly to the nervous system, or the brain, toxicity has been demonstrated. In humans, this has never been done, that I know of. There have been some cases reported of sensitivity to intravenous thiamin.

President Flinn: If the gastro-intestinal tract is in good order, is there any reason for giving thiamin parenterally?

Dr. Goodhart: I don't think so.

President Flinn: Dr. Kaye or Dr. Mackie, how much do antibiotics reduce absorption or otherwise increase the needs for vitamins?

Dr. Kaye: We rarely see vitamin deficiencies in children getting broad spectrum antibiotics over long periods of time. I think that this is due to the widespread practice of supplementing infants' and children's diets with supplemental quantities of vitamins. We see very few cases of chronic intestinal inflammation such as ulcerative colitis and, in these patients, we have not recognized, except in one instance, the presence of frank vitamin deficiency. This was a case of pellagra appearing in a child who was not given supplemental vitamin preparations. I think that, if antibiotics are given for a long time, supplemental vitamins are usually adequate to prevent deficiency states.

Dr. Mackie: We always give Vitamin K when we have anyone on bile drainage, prior to surgery. Periodically people slip through without getting Vitamin K and I don't recall ever having seen anyone develop a detectable profound deficiency from it. I don't think that you would in the short period of time you'd use it to sterilize the bile, unless your patient was in poor nutritional condition before you started.

President Flinn: There are several questions here on stress fortified antibiotics. Are there any purposes to them? Are they all right? Do they do harm? Who wants to speak to that? Dr. Kaye?

Dr. Kaye: We have not taken to these and I think that, for the short-term illness, they are not necessary. For the long-term illness we usually supplement our patients' intake with vitamins, as I mentioned before. I object to this packaging of antibiotics and vitamins. That's probably an emotional reaction on my part.

President Flinn: I am sure you are not alone.

Dr. Goodhart: In the beginning it seemed a little wrong to me, because of the possibility that some of the antibiotics might actually function by interfering with the action of certain of the vitamins. We know that the antibiotics do function by interfering with certain necessary metabolic functions, but it happens that they do not interfere with the particular vitamins present in the commercial combinations. So that there is nothing wrong in giving the combination.

This came up again, as you know, in relation to the treatment of tuberculosis with isoniazid. Patients that were given large amounts of isoniazid developed peripheral neuritis, due to vitamin B_6 deficiency. The neuritis, in tuberculosis patients who had had isoniazid, could be prevented by giving vitamin B_6. Now, of course, the question arose as to whether or not giving vitamin B_6 would interfere with the action of isoniazid upon the tuberculosis organism. Fortunately it has turned out there is no interference with the therapeutic effect of isoniazid.

President Flinn: The only real reason for this medicine is because that when you want to give both it's cheaper, is that it?

Dr. Goodhart: Yes.

President Flinn: What is the physiology which enables thiamin chloride to cure and prevent cramps in pregnancy? I assume it does cure them. Does anybody have anything to say about that one?

Dr. Goodhart: Well, one of the earliest signs of peripheral neuritis is calf muscle tenderness and night cramps. It is by no means the most common cause of night cramps. And I doubt that thiamin is very effective in the treatment of cramps in

pregnancy. It might be in some particular patients who enter pregnancy thiamin deficient and then progress because of increased requirements during pregnancy. The most effective vitamin treatment for calf muscle cramps is calcium pantothenate. Dr. William Bean, while producing experimental pantothenic acid deficiency in man, found that one of the early signs was calf muscle pain and cramps. But there are many vitamin deficiencies which may cause these pains, Vitamin B_6 deficiency does it, pantothenic acid deficiency does it, thiamin deficiency does it, B_{12} deficiency does it.

President Flinn: Well, is a pantothenic acid deficiency state clinically recognizable in man?

Dr. Goodhart: Pantothenic acid deficiency has been produced experimentally in man by Dr. Bean of the University of Iowa.

President Flinn: Thank you. What about vitamin P deficiency?

Dr. Goodhart: There is no vitamin P.

President Flinn: Concerning C complex in habitual abortions. Do you know anything about that?

Dr. Goodhart: No, I don't know.

President Flinn: Do you obstetricians know the answer to that one?

Dr. Mackie: Which one?

President Flinn: Vitamin C complex in habitual abortion deficiency? Well, I guess we'll pass on, then to one or two more.

What mineral supplements, if any, are required by the average 70 year old man in the United States? Is the need related to the rare 70 year old male who elects an inadequate diet, or should everybody have them?

Dr. Goodhart: Seventy isn't so old. One of the outstanding difficulties with elderly people, male and female alike, is to get them to eat sufficient meat and the most common mineral deficiency found is that of iron. I think they are many who believe that the calcium intake of the elderly should be kept high. But whether the rarefaction of the bones commonly seen in the elderly is due to an endocrine disfunction or to an actual dietary insufficiency of calcium is something that still remains to be shown. We also find that the elderly are apt to be deficient in thiamin, vitamin C, and vitamin A.

President Flinn: Well, is there any need for supplemental vitamins for the average individual who is in apparently good health?

Dr. Goodhart: I think you answered that one; you said apparently good health. If you knew him to be in good health, you would have one answer. But apparent good health is something else again.

President Flinn: Do you assume everybody is in poor health then?

Dr. Goodhart: I would say a hundred out of a hundred here are not in perfect health. I think that is the fairest statement. There is something wrong with all of us. Whether we need vitamins would be hard to prove. But, would you say to a person "you're in pretty good health; don't worry about your diet."? I know you all follow certain dietary rules and restrictions to keep yourselves in good health.

President Flinn: Does deficiency of vitamins have anything to do with aphthous stomatitis, the common canker sore?

Dr. Goodhart: Nothing whatsoever.

President Flinn: Are there any other questions?

Voice: Where does the iron go in an elderly person, assuming no blood loss? You say they are iron deficient, if I understood you right.

Dr. Goodhart: The idea that the adult male does not lose iron if he doesn't have blood loss is fallacious. Dr. Carl Moore, using radioactive iron, has demonstrated definite and distinct iron loss in the adult male. He loses iron every time he loses a finger nail, every time he sheds skin, every time he perspires; every time he loses a hair he loses some iron. He loses from 0.5 to one milligram of iron a day. Dr. Moore also has calculated that, if a man were on a diet that contained zero iron and his iron stores were good when he started, it would take something like six years for him to develop an iron deficiency anemia. That's a long time. But a chap whose absorption is not so good, on a diet low in meat and green vegetables, can over a period of several years develop an iron deficiency without gross blood loss.

President Flinn: Thank you very much, but I think we will have to close the panel. We are certainly indebted to all the members.

SOME ESSENTIALS IN OFFICE PROCTOLOGY*

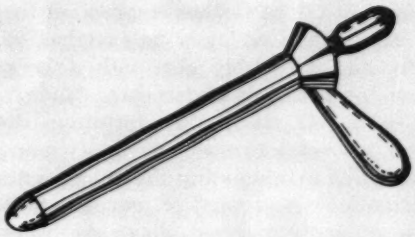
SAMUEL MCLANAHAN, M.D.,**
Baltimore, Md.

In careful clinical work, diagnosis becomes the first responsibility of the examiner. When there are symptoms relating to the colon or the anorectal area, and indeed in most instances of a thorough physical survey, a painstaking examination of this region becomes imperative, serving as it does to rule in or rule out the diagnosis of certain important pathological conditions.

A thoroughgoing examiner will secure the appropriate history, he will make certain systemic or general examinations, he will go over the abdomen, and then inspect the anorectal area and carry out palpation. Today I believe the careful examiner will use, in addition to his index finger, an anoscope or short proctoscope. Whether he elects to carry out proctosigmoidoscopy in his office, or elects not to do so will be his own decision. However, just as he does have x-ray diagnosis available, so must he either be prepared to examine such patients himself or to refer them to a colleague for this important endoscopic examination.

Before drawing attention to some of the more elementary features in reaching a diagnosis in this field let me put in an earnest word for the more frequent use of sigmoidoscopic examination. What can we hope to discover? What chances do we have of making a real "find"? It has been established (Fig. 1) that with the sigmoidoscope, one can expect to diagnose more than 95 per cent of ulcerative colitis, 75 per cent of the polyps of the colon, and at least 70 per cent of the carcinomas of the colon. This is convincing evidence.

Considering for a moment the diagnosis of colonic lesions proximal to the region seen by the sigmoidoscope, barium enema studies must frequently be employed.



CAN LEAD TO
DIAGNOSIS OF

A. UPWARDS OF 90 PERCENT OF ULCERATIVE COLITIS
B. 75 PERCENT OF COLON POLYPS
C. 70 PERCENT OF COLON CARCINOMAS

Fig. 1, Illustrating importance of proctosigmoidoscopy.

While extraordinarily helpful in finding carcinomas and even polyps, this examination is occasionally misleading and must not be given more than its due share of credit. Fig. 2 shows a pedunculated polyp which had been the origin of rectal bleeding, unexplained until the lesion was visualized after several attempts with an air contrast barium study. The polyp was removed by laparotomy and colotomy.

One fact which most of us know well, but occasionally forget, bears repeated emphasis. It is that the x-ray examination cannot be depended upon to visualize the

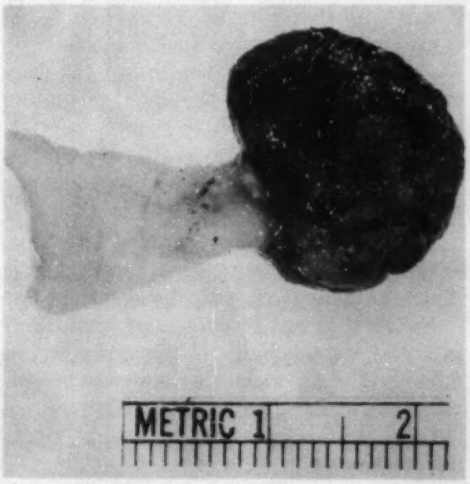


Fig. 2, Adenomatous polyp of sigmoid colon, diagnosed by air contrast barium studies, and removed by colotomy.

* Read before the Medical Society of Delaware; Dover, October 12, 1954.
** Assistant Professor of Surgery, Johns Hopkins University.

rectum. Let it be further emphasized that this area should certainly be examined digitally and preferably also with a 'scope before the enema is undertaken. Radiologists have told me of their fortuitous discovery of rectal tumors, previously unnoticed, while manipulating the tube for the examination. And most of us could recite cases of sadly delayed diagnosis, where barium enemas were reported negative and rectal examinations were too long omitted. The importance of a careful digital rectal examination is emphasized by at least two old cliches, carried down from medical school days: "If you don't put your finger in the rectum, you are likely to put your foot in it!", and a slightly more elegant one: "The chief function of the consultant is to do a rectal examination!".

With regard to the preliminary inspection, one can expect with a good light and with the patient in the knee-chest or even in the lateral position, to be able to diagnose accurately a large group of lesions. The "ghost-like" skin of anal pruritis, the external openings of pilonidal and perianal fistulae, the blue dome or the edematous cap of a thrombosed hemorrhoid, and the almost sealed anal canal protecting the acute fissure, are among the common findings.

The digital examination, in addition to discovering the occasional benign or malignant neoplasm, yields immediate information about the state of contraction — or contracture — of the sphincter mechanism, the condition of the prostate, and the presence and character of the stool. Which of us has not discovered a rectum literally packed with hard fecal matter which has served as a startling explanation for acute and alarming abdominal pain in a child?

Biopsy for laboratory study, and stool examination, represent other approaches to diagnosis which can only be mentioned.

Hence it is to be concluded that there is a real responsibility of diagnosis in this field, and that with the relatively simple measures at hand, employed with a conscientious approach, serious omissions should not be made.

Attention may now be directed to some of the specific anorectal conditions which may be encountered and to a consideration of their origin, recognition, and management.

One of the more recent and widely accepted concepts in proctology has to do with the *origin of anal infections.* Research carried out years ago and more recently confirmed and emphasized, indicates that the preformed anal ducts and glands, occurring in certain individuals, play an important role in the development of anorectal inflammatory disease. As long ago as 1880, Herrmann and Despasses wrote: "From a surgical standpoint these long, tortuous ducts, marked at their extremities by small follicles, present a certain interest, particularly with regard to the role they can play in the production of complicated fistulas which one encounters so frequently in this region." Nesselrod in his text "Proctology In General Practice" states the case clearly for this concept. He even includes hemorrhoidal disease as one of the sequellae of this type of infection. Figs. 3 and 4 from Nesselrod's book illustrate well the sequence of events.

Let us consider for instance, the formation of an *abscess.* The infected material

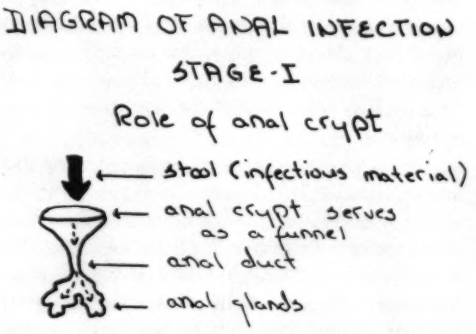


Fig. 3, Origin of anal infection (After Nesselrod).

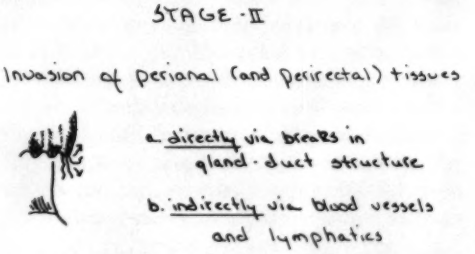


Fig. 4, Origin of anal infection (After Nesselrod).

has burst beyond the limits of the anal ducts and their glands and is starting a true infection. Purulent material begins to form and accumlate promptly, and the future progress of the abscess, and indeed the proper treatment will depend upon the direction it takes. As a matter of fact, the large majority of abscesses arise from a posterior source — a 12 o'clock crypt, in the knee-chest position. A lot of pretty drawings appear in different texts showing usually the cross-section of an anorectal region afflicted with a group of different abscesses. The important point that is stressed is that an abscess may be "deep", that is, above the levator muscle, or more superficial, below the levator muscle.

Wherever it is, the patient will experience increasing pain and the examiner can usually determine the general location of the abscess. Usually there will be induration, redness and tenderness in the perianal area. Less often the abscess may present as a submucous one, being felt digitally as a bulge into the rectal ampulla. Experience has shown that perianal and perirectal abscesses have a peculiar characteristic — they tend to suppurate early, and by the time they are felt as hard, tender swellings they contain an appreciable amount of pus. This gives the key to the proper treatment, which is *prompt incision and drainage.* There need be no waiting for the area to "ripen" or to become fluctuant. The operator will almost always be rewarded with pus. Otherwise, the infection extends in other directions, the fever and disability increase, and what was originally a small abscess may now become an extensive one. If I were seeking for a cause to criticize some of my medical colleagues it would be on this very score. The delay in sending the patient for surgery is often compounded by the administration of antibiotics in a futile effort to abort the already estblished abscess. There is no need to labor the point further; open them early!

While at least half of the abscesses can be expected to heal slowly and surely, the remaining ones will heal down only to a small opening and will persist as *anal fistulae.* It is well to recall that fistulae may be internal as well as external, that they may be simple or very complex. The fistula which results from an abscess may be any of these. The important thing in a new patient is to recognize a fistula; careful inspection and gentle probing are essential. Many small fistulae with short bridges of skin over them can be readily incised as office procedures. The management of the larger fistulae constitutes a surgical chapter in itself.

Fissures or anal ulcers probably result from crypt infections, too. The very acute ones defy examination and diagnosis, and occasionally require emergency hospitalization. But many of them will respond to conservative measures including sitz baths, local applications, and diet. I am sure that we have all experienced disappointment either personal or vicarious for our patients in the use of local pain-relieving ointments. Cocaine happens to be my favorite, but even this fails to bring relief all too often. Authorities differ upon the advisability of injecting the long lasting anesthetic combinations beneath a fissure, many feeling that if this becomes necessary, operation should be undertaken. On the other hand, experience has shown that such a product as nupercain in oil (and there are many others), preceded by novocain, can often save the day, for a while at least, and send a miserable patient away happy. If no complications ensue, complete healing will often take place.

Most of the patients who present themselves with the complaint of rectal bleeding have *hemorrhoids.* But it becomes the responsibility of the examiner to determine in so far as he can whether the bleeding is coming from the hemorrhoids, and in any case, whether there is an associated ulcerative or neoplastic lesion. With modern cancer education we all see frightened individuals who come to consult us, as they are instructed to do, following the appearance of blood from any orifice. They deserve our careful consideration.

Let us consider the management of hemorrhoids. Many patients have clearly demonstrable yet asymptomatic hemorrhoids, with no bleeding, no protrusion, and no pain. It is generally conceded that these individuals do not need surgical treat-

ment. The patient with asymptomatic hemorrhoids, as well as the one with symptoms, may often inquire about his predisposition to cancer. There is no evidence to my knowledge that hemorrhoids give rise to cancer and I believe that the cancer argument should not enter into the reasoning about operation. However, we are all aware that hemorrhoids and cancer of the rectum occur simultaneously more often than might be expected, and that all too many cancer patients have had a hemorrhoidectomy (which failed to stop their bleeding) a short time before their cancer operation.

For the patient with mild symptoms, occasional bleeding and some irritation, an astringent ointment usually containing tannic acid ointment in 5 per cent amounts is likely to be helpful. Where bleeding is the compelling symptom and there is no gross protrusion, injection therapy has proved most successful. After a little study and practice it can be readily carried out by individuals interested in doing so. The technic is relatively simple and the details are described in many texts and articles. The proper selection of patients is most important.

Formal *hemorrhoidectomy* is reserved for those with symptoms of a degree that warrants operation, and where a redundancy of skin and mucous membrane can be demonstrated. This operation has a bad reputation with the public in many quarters, and it cannot be denied that occasional patients will have a painful experience. However, with proper preparation, with attention to detail by the surgeon, and an avoidance of trauma and packing, most patients come through far more comfortably than they had anticipated. A period of postoperative observation, often extending for six weeks, helps to insure the optimum result.

Thrombosed hemorrhoids represent a common complication of hemorrhoids, and are the painful rectal lesions for which patients seem most frequently to consult their doctor. Let it be emphasized that this phenomenon is not an intravascular clotting as the term implies, but is actually an anal hematoma. A vein has ruptured and bled beneath the skin or mucous membrane, and the presence of this free (though often clotted) blood accounts for the bluish cast so often seen, and at other times obscured by the resulting edema. If the areas are multiple or if they are really large, hospitalization is often recommended. The smaller one, however, is easily relieved by the use of novocain, a pair of pick-ups and scissors. The cap can be clipped off, the clot evacuated and permanent relief had by the patient. In other instances the operator may elect to excise the little mass altogether. One error in the management of these painful swellings is often committed not only by the lay people, but also by the profession. That error is to try digitally to reduce or "replace" the swellings within the anal orifice in instances where they actually arise from without. It is true that internal thrombosed hemorrhoids may prolapse and require reduction, but most thrombosed hemorrhoids arise external to the sphincters.

Reference has been made earlier to the diagnosis of *polyps* in the colon and rectum. Evidence is rapidly accumulating which emphasizes the extreme importance in cancer detection and in cancer prophylaxis of finding and eliminating these lesions. They are probably on a par with similar lesions in the bladder. It has been variously estimated that 7 to 10 per cent of the adult population has or will have adenomatous polyps of the colon and rectum. When found, they must be removed or destroyed by one means or another, and their microscopic pathology must be carefully studied. There are a group of these adenomatous polyps which show evidences of malignant change. When the change is limited to the peripheral part of the lesion and does not invade the base, evidence from a number of studies fortunately indicates that the "adenoma malignum" may be safely removed without sacrificing the adjacent bowel. Such a decision, however, requires careful clinical and pathological appraisal.

There are many other important conditions in this area which deserve our attention and discussion, but time necessarily limits the presentation. In conclusion, there has been emphasized the responsibil-

ity of the examiner in suspecting, diagnosing, and managing lesions in the colon and anorectal area. The origin of anorectal infections has been reviewed and the early drainage of suspected abscesses has been advised. Fistulae, fissures, hemorrhoids, and polyps have been briefly discussed and some therapeutic suggestions offered with regard to them.

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DISCUSSION

DR. E. M. AIKMAN (Wilmington): That was a right inclusive paper: it doesn't leave much for me to say. I appreciated the points that were brought out. About all I can do is re-emphasize a couple of things.

I am very glad to hear the doctor suggest more use of the sigmoidoscope, because so frequently we find cases in the hospital who are perfectly worked up and then sort of as an after-thought, on Saturday night or Sunday morning, the doctor calls up and says the patient has been in two weeks; " I wonder if you would have time to go take a look."

Just a week ago I saw two cases of cancer; each patient had been two weeks in the hospital, but as an afterthought they wanted me to look in the rectum.

Then, too, we run into difficulty sometimes with the x-ray man, who tries to crowd it all in together, to get them all cleaned out, and they want the x-ray work, and barium enema and the scoping done at the same time. If we sigmoidoscope them the x-ray man says we produce a lot of spasm in there. Then the reverse is true, because he fills them up with barium and we can't get a look. Neither should be neglected.

I would like to bring out another point that a little care should be taken in making a digital examination. Many times we will find patients who are made quite uncomfortable following a digital examination. If there is any pathology around the rectal-anal region at all the sphincter is tightly contracted, and if the sphincter is forceably dilated something happens. You usually get tearing at the mucosa and the patient is made quite uncomfortable. I think the best way to do it is to let the finger fall into the anal canal rather than actually being forced in to it.

Another thing is the submucus abscess which is frequently overlooked. The patient will have all the symptoms of an abscess, except the visible signs — no swelling, no induration — and yet a digital examination will elicit the bulging mass in the rectal canal. Frequently, because there are no visible signs, that digital examination is overlooked.

I agree with the doctor, too, on the use of injection treatments, but only in very selective patients, and only in the patient that is told definitely that it is palliative treatment, and is not a permanent cure.

One of the rather difficult problems that we have to contend with, I think, are the cases where there is mild infection of a crypt, so mild that it is pretty difficult to determine by palpation or even by direct vision through the anoscope. Yet the patient is disabled definitely; becomes nervous, upset, and soon develops a phobia, yet the symptoms are all out of proportion to the physical findings. I think it is well worthwhile, where the patient is in that condition, to study the case pretty carefully, rather than just put the patient in the category of being a "neurotic".

DR. H. V. P. WILSON (Dover): We all enjoyed Dr. McLanahan's paper, and appreciate his coming over. I don't have many things to discuss about it. It was accurate, and covered the ground fully.

Over in the country every once in a while we are troubled with gas bacillus — farm wounds, and so on. People in the country it seems are coming in contact with gas bacillus more than you do in the city, and every now and then some of us have had bad cases of gas bacillus in perirectal abscesses, spreading up even to the abdominal wall, and before the antibiotics you were hard put to take care of the patients. With the perirectal abscess there was the story of its rapidly extending — a huge thing, and of course if there was crepitus you must expect gas. It is opened widely

and at the same time we routinely take a milk culture and seal it up with a little liquid vaseline, to see if it actually is the gas bacillus. Of course, with the antibiotics, it is different.

Dr. McLanahan mentioned fissures, but I wanted to ask him about the treatment. Some surgeons would dilate the bowel and excise the fissure. That is all right, but I just never knew why, if you simply excised the fissure, the raw place would necessarily want to go ahead and heal. The old treatment of the partial division of an external sphincter doesn't cause any incontinence — I mean, the next morning, if they have a movement, they have it with comfort. If you partially divide the external sphincter it will give relief.

Then, too, I would like to ask about pruritis ani: of course, the cause for it, as far as I know, has never been found. The skin is characteristic and these patients are pretty miserable, especially at night, and the treatment is notoriously bad. They put on any salve anyone happens to know about, and the patients keep scratching.

I have been lately fairly convinced there are two kinds — one, the ordinary pruritis; the other due to chronic fungus infection. Now, that is hard to prove, but there is a proctitis with it, and a history of fungus. As to the ordinary pruritis ani, I have never found any salve that would do any good, more than just for a few hours. I think everybody finally came around to alcohol injections, and then there is a little question about how much alcohol to use, but it will kill the nerve endings and give relief immediately. I think if you use it you have to use enough alcohol; otherwise your patient is quickly itching again. Yet if you use enough alcohol you run into the danger of getting a slough and sterile abscess, and the patient is going to fuss about that.

At any rate, it seems the old treatment with alcohol injections is still the best, until Cortisone came along. I want to ask about your experience with ointments containing Cortisone. Do you know anything about such things, except what I can read in the pamphlets? I see there are some that are highly recommended, and, if they are of any permanent value, that would be a wonderful thing.

The only other thing is about injection treatment of hemorrhoids. I don't know who scared me off about injection treatment of hemorrhoids. I think somebody said it wasn't a good thing to do, and since then I never have done it.

I know somebody who had a treatment with injection of alcohol in another district and he came down with a hard slough, and that further delayed my using the injection for hemorrhoids.

My feeling about it is that it is a little bit like the injection treatment of varicose veins, which I think is pretty well on the way out because of recurrence and because you get so much more satisfactory results from a natural removal.

DR. JAMES BEEBE, JR. (Lewes): I just want to ask what does he do with systemic pruritis, without much evidence of the disease?

DR. O. V. JAMES (Milford): What is the experience with injection of nephrocaine after a hemorrhoidectomy?

DR. MCLANAHAN: I want to thank Dr. Aikman and Dr. Wilson and the others for their remarks.

Dr. Wilson has raised a number of questions. The question of gas abscess is of course an interesting thing and a very rare one. I remember as a house officer seeing an extensive gas-forming infection, and subsequently it was proved bacteriologically to be the colon bacillus, which, under certain circumstances can certainly produce gas, just as the more serious gas organisms can, and they are wretched infections when they come, but I think they may be due to a less benign organism, namely, the colon bacillus, and may not be the true gas gangrene.

With regard to fissure, and so on. The question was raised as to the operation of the fissure, and you wonder if we cut one ulcer out and leave another why we should be any better off.

If we hark back to the etiology, with the wide excision we eliminate an anatomic factor that may be initiating the fissure and give it a chance to heal up. It is one of the things in surgery that has been some-

what empiric in its use. It has worked and does work, and so we do it, but I think anyone working in this field will still have occasionally a fissure which is excised and it again approaches another fissure. Actually, I don't think we have to operate on so many fissures. If you nurse them along many of them will heal up.

The question of pruritus is a big chapter in itself. I couldn't discuss the whole works. That is another subject, in itself. Certainly there must be a lot of kinds of pruritis — some associated with diabetes, some that are allergic manifestations, some that are certainly fungus infections, and some that are entirely idiopathic, as far as we know. Many times they occur in an individual that might have a peptic ulcer. So it would seem to be one of those systemic manifestations or manifestations of some systemic disorder. Again, not so many of those patients have come to the operating room. If they have other pathological changes these should be corrected—hemorrhoids, fissures, or fistulas, and many times the pruritis will be cured.

As to ointments. There are many applications of ointments, and fungicidal ointments are effective in certain groups, and certain ointments have really been dramatic, but there is little prediction. The Cortisone type ointment has been very dramatic at times. I have had some successful experience with it, but I believe you can't just slap the ointment on, and let them go: you have to give other directions and correct any other pathology. It is an aid and a help. It is certainly very expensive for any prolonged use.

Recently, a house officer had been reading the literature, and left an order for the patient that had broken out all over with allergic reactions. I happened along and we sat down and figured that it would cost $50 to get enough ointment for the skin of his whole body.

Alcohol injections have held up, where other things fail, as the final thing to do. And Dr. Wilson described in general the technique and procedure of alcohol injections, which certainly interrupts the train of events and allows the patients to get better, although, unfortunately, not always permanently. We need not go into the technique of that.

With regard to the injection treatment of hemorrhoids, I would like to emphasize again that it is to be used for those people whose only symptom is bleeding. Sometimes you can see an internal hemorrhoid that appears vascular and we have had a lot of success with the injection treatment, warning the patient, as Dr. Aikman suggested, that they may have a recurrence, but it is worthwhile to try. I have had no unfortunate sloughs from injection of hemorrhoids.

Dr. Wilson spoke of injecting the hemorrhoid with alcohol, which is not the substance ordinarily used. I have used quinine urea-chloride, in 5 per cent solution. It differs from the treatment of varicose veins, because the material is not put into the vein but around the vein, and sets up a certain amount of fibrosis there. It has a limited but very useful field.

The final question had to do with the patient that has, shall we say, rectal symptoms, without any demonstrable hemorrhoids. Possibly that patient falls into the important group of those that have cryptitis, and as Dr. Aikman mentioned, there is really very little to be found but there is some residual infection.

Those patients are treated with an astringent ointment, Sitz baths, and care of the bowels. If they do not respond I think operative treatment is indicated, at which time a careful exploration of the crypts and anal canal can be carried out and usually the offending site can be seen.

ESSENTIALS IN THE DIAGNOSIS AND TREATMENT OF CARCINOMA OF THE PROSTATE*

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The physician who undertakes the conscientious treatment of any disease should, before the institution of therapy, have a thorough knowledge of all the information at present available in respect to the etiology, the natural history, and evolution of the particular pathological process presented by the problem with which he is faced.

* Read before the Medical Society of Delaware, Dover, October 12, 1954.
** Associate Professor of Urology, Johns Hopkins University.

Definite causative factors in the origin of carcinoma of the prostate remain unknown, just as they are in neoplasms affecting other locations in the body. Irritative factors, which are of etiological importance in certain tumors in other locations in the body, are not of any importance, as no relationship has ever been established between such conditions as chronic prostatitis or calculi in respect to prostatic cancer. Endocrine factors must play some part, as of course the stimulating action of androgens on prostatic cancer and the inhibiting effects of estrogens have been well established. In certain cases small foci of malignant disease may remain in the prostate gland apparently inactive and it is to be presumed that some endocrine stimulation is responsible for their growth and their transition to clinical cancer.

The frequent occurrence of carcinoma of the prostate has been brought to our attention by pathological studies by Rich, Moore, and others. These studies of series of postmortem examinations have demonstrated that approximately 20 per cent of men over the age of 50 have microscopic evidence of carcinoma of the prostate. Certain writers with a proclivity for statistics have therefore estimated that there are over 3,000,000 men in this country living with carcinoma of the prostate. This fact, of course, could make prostatic cancer the most frequent type of malignant disease in man or woman, but of course vital statistics do not support this statement. The discrepancy between the rate of occurrence and death rate from the disease is explained by the fact that many of these early cancers remain quiescent over long periods of time during which a clinical diagnosis is impossible. The factors which may stimulate one of these quiescent areas to extension and invasion are unknown to us but are probably of hormonal nature.

Pathological studies have demonstrated that in about 80 per cent of cases carcinoma originates in the posterior lamella of the gland, apparently from compressed elements of normal prostatic glands. With the proliferation of the neoplasm the area of origin becomes elevated above the rest of the posterior capsule and also usually assumes varying degrees of induration, some becoming stony hard. It is in this stage that the clinical diagnosis can first be made and if the diagnosis is made at this time the surgical ideal in dealing with all cases of malignant disease, that is, complete eradication, can be attained. As the disease progresses it invades the lateral and median lobes of the prostate and insidiously ascends into the seminal vesicles. Owing to the fact that in these early cases there is no encroachment on the urethra or neck of the bladder in most cases no interference with urination or other symptoms are caused.

Although prostatic cancer originates close to the rectal wall, invasion of this latter structure is extremely rare because the posterior aspect of the prostate and the bases of the seminal vesicles are separated from the rectal wall by a thick fibrous layer, the fascia of Denonvilliers, which embryological studies have taught us is formed by the fusion of the two layers of peritoneum in the lowermost portion of the pouch of Douglas during embryonic development. This fascia is devoid of lymphatics and when it is exposed perineally it presents an unmistakable landmark. The neoplastic cells from the original growth sooner or later invade the perineural lymphatics, extending upward in the fascia around the seminal vesicles, and thence along the lymphatics accompanying the nerve trunks to the bones of the pelvis and lumbar vertebrae, which are usually first to show metastatic deposits on radiographic examination. The metastatic deposits are usually osteoplastic, but osteolytic deposits are not uncommon. With the progression of the disease the prostatic orifice eventually becomes involved and varying degrees of urinary obstruction will develop. In the untreated disease death usually occurs as a result of urinary obstruction and/or ascending urinary infection.

It is obvious, therefore, from these facts that to attain the ideal of complete surgical extirpation the diagnosis must be made before the growth has extended through the capsule or in the fascia surrounding the seminal vesicles. The only reliable method to make such a diagnosis

lies in careful rectal palpation of the whole prostate gland and the recognition of an area in which the induration is of suspicious degree as contrasted with the surrounding tissue of the gland which, under normal conditions, is elastic and compressible. Other disease conditions which may produce an isolated area of induration are (1) prostatic calculi, which can be recognized by radiographic methods; (2) localized areas of chronic inflammation; (3) infarct; (4) tuberculosis. The latter three conditions can usually only be excluded by biopsy and examination of the frozen section.

The extension of the neoplasm is usually so insidious that no symptoms will present and it is only on routine rectal examination that the area of suspicious induration is recognized. Many writers have stated that only 5 per cent of prostatic carcinomata can be diagnosed in the stage early enough to permit complete surgical removal. It is a tragedy only too often encountered to find an extensive carcinoma of the prostate far beyond any hope of complete surgical removal in a patient who has had no pain and no urinary difficulties. It is only by routine rectal examination on all men over the age of forty that these early cases can be recognized. At the Brady Urological Institute in a study of all cases with a diagnosis of carcinoma of the prostate admitted to the hospital between 1937 and 1943, it was found that in 22.7 per cent the radical operation was carried out, but this relatively high percentage of cases suitable for radical extirpation can be explained by the fact that an area of suspicious induration on rectal examination had been found by an alert medical man and the case referred to our clinic for the express purpose of radical extirpation.

It can be stated dogmatically that the hope of salvage of patients affected with early carcinoma depends entirely upon the recognition of the early lesion on rectal digital examination. A dramatic demonstration of this point is afforded by the statistics of Kimbrough from the Walter Reed Hospital. He reports that 54.5 per cent of all patients admitted to the hospital with the diagnosis of carcinoma of the prostate between the years 1940 and 1952 were found suitable for and were subjected to radical perineal prostatectomy. This striking percentage was attained, of course, on account of the fact that rectal examination at periodic intervals is mandatory for all Army personnel forty years of age or over.

For many years attempts to make an early diagnosis of carcinoma of the prostate by needle biopsy have been proposed and nymerous instruments devised. The specimens obtained from these instruments are usually quite small so that accurate interpretation of the stained specimens is difficult. In addition, the technical difficulties of introducing the biopsy needle into the particular small area in the gland which is suspected must be considerable, but besides these two points a much more important consideration must be faced and that is the possibility of implantation of malignant cells in the tissue through which the needle is passed. Let us visualize the procedure; the needle is introduced into a focus of actively growing cancer. In this needle is collected a specimen of viable neoplastic cells. The instrument then is withdrawn through normal tissue of the perineum and certainly some of the cell contents of the trocar must be deposited in these tissues. The fact that cancer cells may grow by implantation is certainly well known to all pathologists, surgeons, and urologists.

We have all seen recurrence of malignant disease in the incision and recti muscles after suprapubic operative procedures on cancer of the bladder and the only answer is implantation of viable malignant cells. That cancer of the prostate can be transplanted has been demonstrated by the experimental researches of Deming, who succeeded in producing active growth of these neoplastic cells in an entirely foreign soil—the anterior chamber of the rabbit's eye. Leadbetter has recently reported a case in which a hard nodule appeared 13 months after perineal needle biopsy in the subcutaneous tissue of the perineum which had been traversed by the needle puncture. The nodule was excised and histological examination showed cancer similar in structure to that previously identified by the needle biopsy and by transurethral resection.

There can be no question that this is an illustration of implantation of malignant cells as a direct result of needle biopsy. Dutra and Geraci have reported a case of needle biopsy of the lung, the specimen obtained showing poorly differentiated carcinoma. Three months later a mass developed in the scar through which the needle had been passed, a biopsy of which showed neoplastic cells similar to the original biopsy obtained from the lung. These are two well documented cases which demonstrate beyond all doubt implantation of cancer cells in the tract following needle biopsy.

In recent years great interest has arisen by the contribution of Papanicolaou on cytological diagnosis of malignant disease. The value of cytological studies has been definitely established in some types of malignant disease, particularly carcinoma of the cervix. Attempts have been made to apply this procedure to the early diagnosis of cancer of the prostate. To obtain material for cytological studies it is necessary to massage the prostate gland with considerable vigor in order to free malignant cells from the suspected area. These cells, when freed, must pursue a tortuous course through the tubules of the racemose glands, finally to arrive through the openings of these glands in the prostatic urethra, and thus to be recovered through the expressed secretion from the urethral orifice. It has long been known that cancer of the prostate extends by invasion of the perineural lymphatics. Would it not therefore be more probable that through forcible pressure on an area of early carcinoma more cancer cells, freed from the original growth by this means, would find their way through the perineural lymphatics rather than through the tortuous course that they must pursue to appear in the prostatic urethra? The necessity of the gentle handling of malignant disease has always been emphasized by surgeons and has been corroborated by experimental research. In 1922 L. E. Knox and later in 1927 M. C. Marsh demonstrated that in experimental mouse cancer a 22 per cent increase of metastasis was produced in those animals in which the experimental tumors were subjected to forcible massage.

The general surgeon who subjects a suspicious nodule of the breast to forcible massage in the hope of expressing material from the nipple for cytological study would be subjected to severe criticism. Certainly we urologists have been taught that suspected malignant disease of the testis should be treated with the utmost respect and palpation reduced to a minimum. Unquestionably forcible pressure on an enlarged kidney suspected of malignant disease in the hope of freeing malignant cells to be recognized as such in the urine would be seriously condemned. From these considerations it is difficult therefore to understand how those who subject early prostatic cancer to the trauma of forcible massage can justify their position. The general surgeon faced with the problem of diagnosis of a suspicious nodule in the breast prepares his patient for possible radical mastectomy, exposes the suspicious area, obtains a frozen section for biopsy, and carries out appropriate surgical measures depending on the microscopic studies.

To those familiar with perineal exposure of the prostate gland, the technique of such exposure offers few more difficulties than those with which the general surgeon is faced in the exposure of a suspicious lesion of the breast. Culp of the Mayo Clinic has recently summarized the problem as follows: "It has been axiomatic that precise diagnosis is a prerequisite of major therapeusis. Many ingenious techniques have been devised for histological studies of palpable nodules in the prostate but only perineal exposure of the gland affords direct access to the entire posterior lamella. Biopsy by way of this route therefore should have the greatest potential for indicating unequivocally the cases suitable for complete eradication of malignant disease by radical perineal prostatectomy. The comparison of frozen section examination and (simultaneous) prostatectomy of appropriate type has no parallel in other diagnostic or therapeutic schemes."

Certain criteria for the selection of cases suitable for radical perineal prostatectomy have been established and it is felt that adherence to these principles is largely responsible for the absence of mortality in our personal series and for the improve-

ment in functional end-results. These criteria can be summarized as follows: First, the area of suspected induration must not extend beyond the capsule of the gland, into the membraneous urethra or extensively involve the fascia around the seminal vesicles, and the whole gland must be freely movable. Second, there must be no demonstrable metatases either on physical examination or more particularly by radiographic studies, and the acid phosphotase determination should be within normal limits. Third, the patient should be a good surgical risk and, most important, his life expectancy must be good. It must be remembered that prostatic cancer is a slowly progressing disease in most cases, especially the elderly, and we cannot condemn too strongly performance of this procedure in an older man whose life expectancy is obviously limited. It has therefore been our custom to reserve the radical operation for patients under 70 years of age, but this requirement is by no means didactic, as exceptions will always be found on either side of this figure.

Advances in our knowledge of the influence of hormones on the growth of cancer of the prostate have proven that in the majority of cases the suppression or withdrawal of androgen stimulation either by orchiectomy or adminstration of estrogens will result in regression of the neoplasm. However, complete eradication of the disease by hormonal therapy alone has not yet been recorded. With the knowledge that most cases of prostatic cancer will show local regression when deprived of androgen stimulation, and in an attempt to extend the sphere of usefulness of the radical operation, it has been our custom to institute estrogen therapy in all cases in which a diagnosis of carcinoma has been made. Dr. Brice S. Vallett was one of the first to publish a case illustrative of this phase of the efficacy of estrogen therapy. His case when first seen was considered inoperable on account of its local extension and fixation of the gland. After a period of estrogen therapy regression had occurred to such an extent that the gland became freely movable and the radical operation was successfully carried out.

When faced with the problem of an area of suspicious induration in the prostate gland it has been our custom to prepare the patient for radical operation, to discuss this possibility with him, and also to tell him that if the radical operation is carried out sex power may be markedly impaired or completely destroyed. The prostate is exposed through the perineum, the suspicious area identified and excised and frozen sections immediately studied. If several sections fail to show malignant disease the wound is closed, unless an accompanying hypertrophy with urinary obstruction is present. If the sections show definite carcinoma, the radical operation is then performed.

Complications at the operating table are usually extremely rare. It is not the purpose of this presentation to enter into technical details, but bleeding is satisfactorily controlled by early ligation of the lateral ligaments. The bleeding from the bladder wall is also controlled by the suture with which the bladder defect is closed. In fact, in our experience hemorrhage, both primary and postoperative, is far less frequent in cases subjected to radical operation than in those in whom enucleation of a benign adenoma has been performed. Injury to the rectum is a possibility, but has not occurred in this recent series. If recognized, the rectal injury should be closed by two layers of sutures. Immediate fall in blood pressure is usually easily controlled by intravenous fluids, and if an unusual amount of blood has been lost this should be replaced by transfusion. Postoperative infection is controlled by antibiotics. The urethral catheter is usally left in place for about ten days. Leakage through the perineum may occur, but we have had no cases of a persistent perineal urinary fistula. Some degree of incontinence of urine is often present in the first days after the catheter has been removed, but control is usually promptly regained if the structures of the external sphincter have not been injured during the operation. Often difficulty in control will be found to result from a constriction at the site of anastomosis between the stump of the urethra and the bladder, and this can be easily corrected by gentle dilalations.

With improvement of operative technique, especially care in placing the sutures anastomosing the stump of the urethra to the neck of the bladder so that no knots are tied over the muscles of the external sphincter, there has been a progressive diminution of postoperative permanent incontinence. This condition has been arbitrarily defined to include any patient who finds it necessary to wear any sort of apparatus during the day a year or more after operation. In a series of 15 cases operated upon prior to February, 1943, urinary control was classified as good in 12 cases, poor in 3 — 20 per cent. Of 34 cases operated upon between February, 1943 and February, 1948, urinary control was poor in 6 —17.1 per cent. In 44 cases in which the operation was performed after February, 1948, control was classified as poor in 3 — 6.6 per cent.

In a personal series of 99 cases there has been no operative mortality, a fact which may be attributed to strict adherence to the criteria for operability which have been previously detailed. Antibiotics have undoubtedly played a most important part in preventing postoperative infection and the complications which may follow; but, on the other hand, a number of these cases were operated upon in the pre-antibiotic era.

A total of 49 personal cases were subjected to the radical operation prior to 1948. Of these 20, or 40 per cent, are living and well without evidence of recurrence or metastasis. If, however, 8 deaths from other causes are subtracted, this percentage rises to 49. This figure is in close agreement with others (Young, Lewis, and others) who have studied survival rates after radical perineal prostatectomy. In a study of the statistics at the Brady Urological Institute, Jewett found that the ten-year survival rate was 28 per cent and emphasized that the ultimate prognosis was far better in those cases which on examination showed no apparent extension of the neoplasm beyond the prostatic capsule. Jewett also stated that "no patient who lived 10 years without demonstrable recurrence or metastases subsequently showed evidence of cancer."

When the patient is discharged from the hospital it is usually our custom to prescribe estrogens in small doses for several months in the hope that if viable cancer cells are still present after the radical operation they may be inhibited or even destroyed by estrogen therapy.

When recurrence of the neoplasm occurs following the radical operation it usually first appears between the bladder and the rectum and well above the site of the anastomosis between the bladder neck and the stump of the urethra. In this location it causes no obstruction to the urinary passage and does not invade the bladder wall or the rectum, as the growth follows the easiest pathway via the retroperitoneal structures. Under these circumstances death ultimately occurs from carcinomatosis and the patient is spared the pain, urgency, frequency, and hematuria from encrusted cystitis and necessity of repeated transurethral resections which so often occur in the natural course of the disease.

A case which clearly illustrates this point was that of a 60 year old man on whom radical perineal prostatectomy for early cancer was performed in 1926. His recovery was uneventful and normal urinary function and perfect control were speedily regained. He remained well until four years after the operation when a nodule was detected high up between the bladder and the rectal wall. This caused no interference with either bowel or bladder function and urinary control was complete until his death from coronary thrombosis fourteen years after the operation. No estrogens had been administered and orchiectomy had not been done. On postmortem examination a nodular mass was found in the loose tissue between the bladder and the rectum, neither of which structures were invaded. Study of sections of this mass demonstrated an adenocarcinoma identical in structure with the original neoplasm which had been removed fourteen years previously.

When local recurrence is demonstrable, no matter what interval of time after the radical operation, our present plan is to institute estrogen therapy and continue this treatment indefinitely. If there is evidence that the recurrent neoplasm is in-

creasing in size or if metastatic deposits are demonstrable by radiological studies and especially if pain becomes progressively more severe, orchiectomy should be done.

As is well known, the progress of prostatic cancer, whether it be primary or recurrent after operation, can be effectively controlled for varying intervals of time by hormone thereapy in approximately 80 per cent of cases. However, sooner or later, in the course of this treatment evidences of progression of the primary neoplasm occur, often with reactivation of areas of metastasis and usually pain becomes progressively more severe. This stage of the disease is commonly called the phase of relapse or reactivation. Bilateral adrenalectomy has been proposed and carried out at this stage by numerous surgeons with temporary relief of symptoms and improvement in general condition, but the operation has now been generally discarded because it has been demonstrated that approximately the same benefit can be obtained by the administration of Cortisone, the so-called "medical adrenalectomy." It must not be forgotten that when intractable pain is present, which cannot otherwise be controlled, deep x-ray therapy may often afford great relief.

Extensive studies are at present being carried out in several clinics on the use of radioactive isotopes in the treatment of prostatic cancer, but these methods are still in an experimental stage and recent reports indicate that their use is not without certain dangers and unfortunate complications. As yet, no reports of complete eradication of cancer of the prostate as a result of therapy with radioactive isotopes have appeared, but some years must elapse before the value of these methods can be accurately evaluated.

SUMMARY

The essential facts regarding the origin and extension of carcinoma of the prostate are discussed and emphasis is placed upon the fact that in the early stages the neoplasm may remain entirely within the capsule of the gland. Under such circumstances it is entirely feasible to attain the surgical ideal in dealing with malignant disease — complete excision. Early diagnosis depends entirely on rectal palpation, which should be a routine procedure in the physical examination of every man over the age of 40 years. If the patient is in good condition and has a good life expectancy the prostate should be exposed perineally, a frozen section biopsy made and, if positive for malignant disease, the radical operation should be forthwith carried out. Other methods of early diagnosis, punch biopsy, and cytological studies are simply mentioned to be condemned.

The great value of hormone therapy, either by administration of estrogens or orchidectomy in controlling the progress of the disease and relieving pain, has been discussed. By either of these two methods it is sometimes possible to cause such regression of an otherwise inoperable case to render the radical operation technically possible. Bilateral adrenalectomy has been carried out for inoperable cancer of the prostate in many clinics, but has now been discarded, as essentially the same results can be obtained by the administration of Cortisone — the so-called "medical adrenalectomy".

The treatment of extensive cases of carcinoma of the prostate by radio-active gold or isotopes is still in an experimental stage, but this technique offers hope that it may be very valuable in otherwise hopeless cases.

In the present state of our knowledge, the radical total prostatectomy with excision of the gland in its capsule and the seminal vesicles offers the best prospect at present available for complete eradication of the disease.

Brady Urological Institute, Johns Hopkins Hospital

DISCUSSION

DR. B. S. VALLETT (Wilmington): It is a privilege and honor to discuss this timely and important paper.

Dr. Colston, long associated with the late Dr. Hugh Young, caught up the fire of his dynamic teacher and has relentlessly pursued the task of education in this sadly neglected field, viz: the early detection of prostatic cancer. That his task has not been wholly unrewarding is attested by the fact that the September issue of the *Journal of Urology* carried no less than ten papers relating to this problem by various workers in widely separated areas of our nation.

This, however, is not primarily the problem of the urologist, as he sees but a very small percentage of the male population as compared to his medical brothers in the various fields of medical care. His special knowledge, however, should be more widely utilized, as Kaufman, Rosenthal and Goodwin state: "The detection of early carcinoma depends upon frequent intelligent palpation of the prostate".

The late Nelse Ockerblad, the eminent urologist, once remarked that the average case of prostatic cancer seen by the urologist had had the disease for 3 or 4 years. What an excellent opportunity is afforded all physicians who do routine physicals on men over 35 years of age to ferret out this insidious disease. We must learn to think more in terms of cure and fully realize that it is "the man without urinary symptoms" that we must suspect as harboring the disease, as he represents the ideal case for potential cure.

I doubt that anyone has even the remotest idea as to the percentage of physicians that now do routine digital rectal examinations of their male patients, however, it is not too much to hope for the ideal 100% in the not too distant future and in its fulfillment we shall witness the conclusion of one chapter of "the urologists' dream".

DR. E. L. STAMBAUGH, (Lewes): I feel that Dr. Colston has ably shown that the urologist has kept pace with his surgical friends in the early diagnosis of carcinoma. Dr. Colston, along with others, has pointed out that we cannot rely upon the clinical investigation alone, in the diagnosis of carcinoma of the prostate.

A medical history is often inadequate in enlightening us as to suspicious cases, and hematuria so frequently is absent in the early benign carcinomas of the prostate, which occurs later in the malignant. In finding such a nodule it is of course necessary to investigate further to suggest open perineal and surgical biopsy.

I would like to inject maybe one point: We have seen carcinoma of the prostate left behind after encleating a hypertrophied prostate gland and I feel these patients, these prostatectomized patients, should have cancer check-ups.

Finally, the subject nears completion when we can still do something for the "stoney heart". Estrogens and orchiectomy, hailed some years ago, are still our only solution for the advanced disease.

DR. COLSTON: I have nothing to add by way of conclusion except to thank Dr. Vallett and Dr. Stambaugh for their remarks.

Constant alertness to reversion to endemic and epidemic conditions is essential, and some situations, especially tuberculosis, require determined and drastic attention, but generally speaking, the public health programs are drifting away from the early ages of high infant and maternal mortality and the communicable diseases toward adult health, chronic disease, cancer, heart, diabetes, nutrition, mental health, and accident prevention. Most of these latter conditions demand sound and knowing participation on the part of the individual and his family. The mass approach alone will not be productive. Henry F. Vaughan, Dr. P.H., Am. J. Pub. Health, Mar., 1955.

Enormous numbers of adult human beings carry tubercle bacilli in a semi-dormant state and hold their infection in check under normal circumstances. However, non-specific physiological disorders can disturb the equilibrium between bacilli and host tissues and convert the latent tuberculous infection into overt tuberculosis. Rene J. Dubos, Ph.D., J.A.M.A., April 23, 1955.

All physicians should be alerted to the fact that case register loads of active tuberculosis are higher now than at any time in the last few years. With the improved therapy of tuberculosis, case loads obviously will continue to be heavy for some time. Tuberculosis, therefore, is far from being a conquered disease. Physicians should regard it as a duty, both in their practice and in their public utterances, to push for adequate and complete eradication of tuberculosis with whatever tools are feasible and available. Michael L. Furcolow, M.D., Editorial, Journal-Lancet, April, 1955.

NEW MEMBERS SINCE JULY 15, 1954

New Castle County — Active

Name	Address	Specialty	Tel.	School	Licen.	Joined
Aikins, James P.	Delaware Hosp.	An*	OL 4-5211	McGill, '45	1949	12/55
Alden, Carmi	Newark, Del.	ObG		Tufts, '19	1955	2/56
Allen, Olin S., II	Reading, Pa.	I		Temple, '52	1953	10/54
Baganz, Herbert M.	1210 Delaware Ave.	I	OL 5-3329	Penn., '47	1951	12/54
Baker, Frank W.	207 S. Maryland Ave.		WY 4-7414	Hahn., '51	1952	12/55
Benning, Charles H.	City Hall	Ph*	OL 8-7121	McGill, '17	1955	12/55
Bishop, Sarah	511 W. 8th St.	Ph*	OL 4-3181	Mich., '32	1955	4/55
Blase, William C.	1009 Delaware Ave.	I	OL 4-9039	Hahn., '47	1948	10/54
Blumberg, Alan I.	1711 Marsh Rd.	I	SY 8-6169	Jeff., '47	1954	3/55
Brennan, Robert J.	1207 Delaware Ave.	Ped.*	OL 4-7712	Jeff., '47	1950	12/55
Dworkin, Albert	1104 N. Jackson St.	Ob.*	OL 5-3500	Temple, '52	1953	12/55
Eskew, Kenneth W.	Brookside Park, Del.		EN 8-4762	Ind., '52	1954	12/55
Esterly, Katherine L.	1415 Delaware Ave.	Ped.	OL 8-7556	Temple, '51	1954	12/55
Gelb, Albert	1100 Gilpin Ave.	S	OL 5-7786	Jeff., '49	1953	12/55
Gross, Elmer R.	Medical Arts Bldg.	D*	OL 5-6869	Mich., '33	1935	9/55
Hall, William T.	1210 Delaware Ave.	I	OL 8-2660	Temple, '44	1954	9/54
Hanel, John H.	1 Alvil Rd.		WY 4-2880	Penn., '50	1953	12/55
Hearne, Calvin B.	114 Murphy Rd.	Ped.*	OL 6-6118	Md., '47	1951	12/55
Heckler, G. Barrett	1406 N. Van Buren St.	I*	OL 4-9511	Jeff., '48	1952	12/55
Hillyard, Raymond W.	1007 Delaware Ave.	Ns*	OL 4-8835	Penn., '46	1953	9/54
Holloway, William J.	503 Delaware Ave.	I*	OL 8-4356	Md., '48	1952	12/55
Huntingdon, Park W., Jr.	Delaware Hosp.	Pa*	OL 4-5211	Jeff., '49	1952	4/55
Lawson, James J.	Nemours Bldg.	In*	OL 4-5121	Tufts, '49	1956	2/56
Levitsky, David A.	1207 Delaware Ave.	Ped.*	OL 4-7712	Jeff., '51	1952	12/55
McCarthy, James R.	1100 Madison St.		OL 2-6144	Hahn., '48	1949	10/54
McGee, Donald H.	1100 N. Broom St.	Ped.*	OL 4-4042	Jeff., '47	1948	3/56
McKusick, Marjorie J.	1302 Delaware Ave.	P*	OL 6-9729	Harvard '49	1953	1/55
Mantell, Harriett B.	Silver Brook, Del.	Ped.	EN 8-4586	N.W.U., '48	1954	3/56
Martin G. William, Jr.	1504 Marsh Rd.		SY 8-0512	Md., '50	1955	12/55
Mekanik, Edwin A.	1100 N. Jackson St.	S*		Hahn., '46	1953	10/54
Potocki, Peter P.	1329 Linden St.		OL 4-0404	Jeff., '52	1953	2/55
Price, Richard H.	Newark, Del.	NP	EN 8-2594	Buffalo, '20	1928	1/56
Sherman, Leo F.	4th & Franklin Sts.		OL 4-8024	Md. Va., '50	1954	12/54
Sisson, William H.	1104 N. Adams St.	P*	OL 4-5432	Vt., '45	1954	12/54
Smith, Caleb H.	604 W. 11th St.	Pr*	OL 6-7468	Penn., '53	1955	5/55
Smith, Glen T.	Nemours Bldg.	In(1)*	OL 4-5121	Chicago, '37	1954	9/54
Tikellis, Ignatius J.	1801 Marsh Rd.		SY 8-0218	Harvard, '48	1955	9/55
Vandervort, Roberts	Wilmington General Hosp.	An*	OL 6-2551	Pitts., '46	1954	9/54
Walker, Earl E., Jr.	Brookside Park, Del.		EN 8-4762	Emory, '52	1954	12/55
Watson, Thomas L.	Newark, Del.	In*	EN 8-7111	Va., '30	1948	1/56
Weaver, Owens S.	1103 Delaware Ave.	ObG*	OL 6-6684	Hahn., '46		12/55
Wendell, Henri F.	Garfield Park, Del.		OL 4-7729	Penn., '53	1954	12/55
Wright, William A.	du Pont Experimental Station	In*	OL 6-3361	Albany, '49	1955	12/55
Wuertz, Robert L.	1117 N. Franklin St.	I	OL 8-5437	Temple, '48	1953	10/54

New Castle County—Associate

Bonnett, John C.	Nemours Bldg.	In*	OL 4-5121	Hopkins, '43		2/56
Cates, Haynes B.	1501B N. Broom St.	O*	OL 6-6679	Tenn., '42	1949	12/55
Sachs, Kurt	V. A. Hospital	I*	WY 4-2511	Vienna, '35	1954	12/55
Sluzar, Oleh O.	Bissell Sanatorium		WY 8-2223	Marburg, '49		1/56

Kent County—Active

Hays, James F.	Latex Corp., Dover	In(C)*	4761	Jeff., '23	1954	11/54
McNinch, James R.	Dover, Del.	S*	7432	Md., '45	1954	3/55
Krieger, John A.	Dover, Del.	ObG		N.Y.U., '51	1955	9/55

Sussex County—Active

Bandy, William H.	Georgetown, Del.	Ph*	2319	M.C.Va., '41	1954	4/55
Henning, Carl (Ret.)	Rehoboth, Del.	O		G. Wash., '05	1948	1/55
Lowis, Robert F.	Seaford, Del.	An		Rochester, '30	1955	11/55
Rizzo, Alessandro	Seaford, Del.	In	3087	Bologua, '33	1954	2/55
Sills, David N., Jr.	Milford, Del.	S*	4053	Md., '46	1954	1/55

Sussex County—Associate

Maresch, A. Emanuel	Lewes, Del.		2211	Munich, '49		4/55
Portz, Warner P.	Milford, Del.	An	4561	Georget'n, '47	1955	4/55
Ware, L. Ulo	Lewes, Del.		2211	Marburg, '48		4/55

NORWOOD W. VOSS, M.D.

Dr. Norwood W. Voss, 70, a past president and treasurer of the New Castle County Medical Society, died of pulmonary embolism on February 17, 1956, at his home, following an illness of about a year.

Dr. Voss was a general practitioner here since 1919. He had earlier worked for the Du Pont Company in Parlin, N. J., for 18 months, and before entering medical school, had been principal of a school in Stevensville, Md., for four years.

Husband of Mrs. Barbara Willis Voss, he was born near Harrington, and was graduated from Washington College, Chestertown, Md., in 1908. Two years ago the college alumni association cited him for distinguished service to medicine.

He was graduated in 1916 from the University of Maryland Medical School, and interned in Baltimore before joining DuPont in Parlin.

Dr. Voss had courtesy staff privileges at all four Wilmington hospitals. He was a member of Lafayette Lodge 14, A. F. & A. M.; Delaware Consistory, Brandywine Methodist Church, the county, state and national medical associations, and the Delaware chapter, American Academy of General Practice.

In addition to his widow, he is survived by two daughters, Mrs. Glenn Getz, Hopewell, Va., and Mrs. David J. Reinhardt, III, Wayne, Pa.; a sister, Miss Anne Voss, and a brother Martin Voss, both of Denton, Md., and four grandchildren.

Funeral services were held in the Spicer Funeral Home on February 19th, with fifteen of his colleagues serving as honorary pallbearers. Interment was on February 20th, at Denton, Md.

JOHN E. ROBBINS, M.D.

Dr. John E. Robbins, 51, former coroner's physician here and a well-known general practitioner, died on February 23, 1956 in the Miami Heart Institute, Miami Beach, Fla.

Dr. Robbins, who had suffered from a heart condition for some years, was appointed in 1954 to succeed Dr. P. A. M. Robitti, following the latter's death in December 1953.

Born in Wilmington, Dec. 21, 1904, the physician was the son of Catherine McClafferty Robbins and the late James P. Robbins. He was a graduate of Wilmington High School and of the University of Delaware and received his medical degree at Hahnemann Medical College, in 1930.

Dr. Robbins served his internship at the Memorial Hospital and was associate-anestheist there. His father was partner in the well-known paint firm of Bamberger & Robbins, Inc.

A member of the New Castle County Medical Society, he was affiliated also with the Medical Society of Delaware and the American Medical Association.

He was a member of Sigma Phi Epsilon, Sigma Kappa Delta, the Druids, the Derelicts, the Wilmington Country Club, and the Benevolent and Protective Order of Elks.

Survivors, besides his mother, include his wife, Mrs. Alice O. Robbins; a son, John C. of this city, who is a student at the University of Delaware; two brothers, James P., Jr., and Willard L., both of this city, and two sisters, Mrs. James Harper of the Germantown section of Philadelphia and Mrs. Harry W. Orth, Hillcrest.

A solemn requiem mass was sung in St. Patrick's Catholic Church on February 28th. Interment was in Cathedral Cemetery.

Editorials

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CHECKUPS

"Fight Cancer with a Checkup and a Check" is the slogan of the American Cancer Society for the coming April fund campaign.

One great hope for this drive is that it will encourage and lead many persons to local and family physicians for a routine physical examination — even those who are apparently perfectly well. This Editorial is written in the hope of acquainting the physician of this coming campaign and encouraging the execution of this examination in response to inquiry by the patient. This endeavor will further extend the physician's office into its important role as a detection center for cancer.

The value of examining apparently well people is obvious; in spite of cost, this has been proven in all fields where it has been tried. Daily we are confronted with cases in which, if the individual had waited until symptoms had become manifested, the situation would have become hopeless or nearly so. Early detection is the only answer and this means extending our examination even more to apparently well people.

To date we have no simple screening method to offer the general public. The biopsy of suspicious tissue remains our only means of evaluating the situation. While the Papanicolaou smear has proved its worth for cervical smears, both in ease of obtainment and in percentage of positive finds, it is of limited value elsewhere, especially where secretions have to be depended upon. Above all, a suspicious mind remains our best tool.

The examination in the office should include a thorough review of systems, physical examination, and minor laboratory tests. The physical examination should include a pelvic, rectal, and sigmoidoscopic examination. The laboratory examination may include a blood count, urine examination, stool for occult blood utilizing the simple guiaic method, and a Papanicolaou smear. The Papanicolaou smear can be screened and processed by the local pathologist for a nominal charge; for indigent patients it can be obtained free of charge. The State Laboratory will gladly furnish the necessary equipment and process the Papanicolaou smear free of charge if desired.

The Cancer Detection Center of the New Castle County Unit of the American Cancer Society, Delaware Division, Inc., to date has detected 79 positive cases of cancer in 8,308 women patients examined in the past 7 years. These persons all assumed that they were well until told of their disease. The examination at the Center is limited to the breasts, pelvis, and rectum. Males are excluded for examination. During this same period of time 5,985 conditions of non-cancerous origin have been detected and referred to their family physician. 5,851 individuals have returned repeatedly for regular examination and have expressed their desire to continue. Many of the women are reluctant at first to obtain an ex-

amination, but after the first one will return for regular examination.

These examinations may easily be incorporated into a routine physical checkup. All male patients should have a rectal examination and palpation of the prostate gland. Male and female patients should have a sigmoidoscopic examination. Through the physician's influence, recognition of the importance of self-examination of the breasts, awareness of the danger signals for cancer, and repeated periodic checkups can be forcefully brought home to the patient.

We heartily believe that cancer detection can be and should be done in every doctor's office and that the physician can do much to impart to his patients the necessity for this repeated examination. Through his contact with his patient and the confidence he enjoys, the physician can bring success to the "checkup" phase of this coming campaign and make it a success at the local level.

It is accepted that tuberculosis is probably the most important disease in the tropics today. It has gone ahead of malaria and sleeping sickness. Yellow fever can be mastered by hygiene and vaccination. Other tropical plagues can be controlled by public health measures. Tuberculosis remains a problem. Harley Williams, M.D., Nat. Tuberc. A. Tr., May, 1954.

The fact must constantly be remembered that no case of tuberculosis can be treated unless it is first discovered. Furthermore, success with the newer forms of treatment, as with the old, is inversely related to the length of time the disease has been present and the degree of involvement when therapy is begun — the longer it has been present and the more extensive the disease, the less effective the treatment. 23rd An. Rep. of the American College Health Assn., Journal-Lancet, April, 1955.

So long as active cases are reported in such impressive numbers, it cannot be assumed that tuberculosis is a conquered disease. Theodore J. Bauer, M.D., J.A.M.A., August 20, 1955.

Now that bovine tuberculosis has been all but wiped out in this country, man himself is the source of practically all infection . . . It can be accepted as a fact that infection with tubercle bacilli commonly results in necrotic lesions which, even though not ordinarily detectable, persist and remain infected for a long period of time. Since tuberculin surveys clearly show that a large percentage of adults have been infected, it is prudent to assume that many of them still carry virulent bacilli. Rene J. Dubos, Ph.D., Nat. Tuberc. A. Tr., May, 1954.

The incidence of persons now harboring tubercle bacilli varies greatly in different parts of the world. In nations with large populations where little effective tuberculosis control work has been done, so many children become infected that nearly all adults possess at least lesions of primary complexes containing tubercle bacilli. Among such people, a correspondingly high incidence of clinical tuberculosis is present. J. Arthur Myers, M.D., Journal-Lancet, April, 1955.

It is the living patients who make up the tuberculosis problem, both as to their treatment needs and the threat they present to perpetuation of the disease. Leo Tepper, M.D., Dis. of Chest, September, 1955.

Public health seeks to have as many persons as possible assume responsibility for obtaining, through their own resources, needed health services. Herman E. Hilleboe, M.D., and Edward R. Schlesinger, M.D., Journal-Lancet, May, 1955.

Programs which stand the greatest chance of further reducing morbidity and mortality rates will be those that require an informed and enlightened public — informed to the extent that the individual has certain attitudes and engages in certain actions because he is convinced that he must take these actions to provide the benefits of good health to himself, his family, and his community. Leroy E. Burney, M.D., Am. J. Pub. Health, February, 1955.

The physician concerned with tuberculosis and diseases of the chest must always be aware of the complications arising from fungus infection of the lungs which may simulate tuberculosis in every degree. Michael L. Furcolow, M.D., Editorial, Journal-Lancet, April, 1955.

The present favorable situation with respect to tuberculosis mortality is the result of modern case-finding techniques, developed some years ago and applied intensively since 1945; and it is the result of tremendous advances in the chemotherapy of tuberculosis. Leonard A. Scheele, M.D., Bull. Nat. Tuberc. A., May, 1955.

BOOK RIEVIEWS

Bickham-Callander SURGERY OF THE ALIMENTARY TRACT—Volumes I, II, and III. By Richard T. Shackleford, M.D., Assistant Professor of Surgery, Johns Hopkins University, assisted by Hammond J. Dugan, M.D., Assistant in Surgery, Johns Hopkins University. Pp. 2575, with 1705 illustrations. Cloth. Price, $60.00 per set. Philadelphia: W. B. Saunders Company, 1955.

Dr. Shackleford in his rewriting of Dr. Callander's review of Bickham's *Operative Surgery* has presented a straight-forward text of which he may well be proud. This work, in three volumes, is an epic worth all the time and effort the author must have put into its production in an age when concepts are so rapidly changing. The planning, illustrations and their descriptions are superb. The books will be of utmost value to the intern, resident, and practicing surgeon for many years and should be in every hospital's library. The only criticism that can be noted is that the text is most inclusive leaving little to the supporting bibliography. The last chapter might well be the first, so that repetition could be eliminated.

The first volume covers the surgery of the esophagus, stomach, duodenum, liver, gallbladder, and extrahepatic biliary ducts. The second volume continues with the surgery of the pancreas, spleen, jejunum, ileum, peritoneum, omentum, mesentery, and colon. The third volume finishes with the anorectal tract, rectum, gastrointestinal hernia, and incisions. The scope of the work leaves nothing for the reader on which to theorize. Its completeness is phenomenal and shows the effectiveness of a surgeon's organized thinking. Congratulations, Dr. Shackleford!

TEXTBOOK OF ENDOCRINOLOGY. Edited by Robert H. Williams, M.D., Professor of Medicine, University of Washington, with ten contributors. Second Edition. Pp. 776, with 175 figures. Cloth. Price, $13.00. Philadelphia: W. B. Saunders Company, 1955.

Perhaps the opening statement of Dr. Williams in his preface to this second edition emphasizes briefly the importance of endocrinology in the present day knowledge of every physician: "The hormones significantly affect the activities of every body cell. They influence the metabolism of carbohydrates, fats, proteins, minerals and vitamins. There are few major diseases that do not influence endocrine function, and vice versa . . . ".

The book, consisting of thirteen chapters, is well illustrated with photographs, tables, and diagrams, and there is a complete index. Bibliographies follow each chapter.

The general principles of the physiology of the endocrines are discussed as they relate to clinical symptoms in animals and in man. The endocrine glands are then discussed in detail, giving the disease entities produced by variations in gland activity, and pointing out the clinical and laboratory diagnoses and treatment. Actual photographs of patients illustrate many of the unusual endocrinopathies.

The chapter on neuroendocrinology will be found full of new and stimulating considerations in that the nervous and endocrine systems are welded together into an enormous complex functional unit.

Of interest to biochemists and clinicians alike are the chapters on laboratory diagnostic and assay procedures; the diagnosis and treatment of endocrinopathies; and hormone preparations. Medical students, too, will find this a valuable textbook. It represents, in short, a wealth of clinical information in a field of medicine which was clouded with mystery and theory only a few years ago. We recommend it highly.

CLINICAL BIOCHEMISTRY. Fifth Edition. By Abraham Cantarow, M.D., Professor of Biochemistry, Jefferson Medical College, and Max Trumper, Ph.D., formerly Lecturer in Clinical Biochemistry and Basic Science Coordinator, Naval Medical School, National

Naval Medical Center, Bethesda, Maryland. Pp. 738, with 54 figures. Cloth. Price, $9.00. Philadelphia: W. B. Saunders Company, 1955.

As stated in their first edition in 1932, the purpose of the authors was then, and is today, the correlation of biochemistry and physiology to clinical medicine.

The dedication of the book to the memory of Albert P. Brubaker brings back happy memories to those of us who were taught by that kindly philosopher and teacher of physiology at Jefferson.

This clearly and concisely written book consists of twenty-three chapters, an index, and an outline of normal chemical standards. Complete coverage is given on carbohydrate, lipid, protein, and nucleic acid metabolism, as well as metabolism of the various chemicals in the body and the function of the various body systems. The last chapter deals with cerebrospinal fluid. References are given at the end of each chapter.

The chapters on sodium, potassium, and chloride metabolism, acid and water balance are especially well presented and augmented by tables which the general practitioner will find of useful application in his daily practice.

Unquestionably, this is indeed a valuable addition to every physician's library, and in particular to that of the family physician, who must constantly evaluate physiological and biochemical problems.

CANCER CELLS. By E. V. Cowdry, Ph.D., Director, Wernse Cancer Research Laboratory, Washington University, St. Louis. Pp. 677, with 137 figures. Cloth. Price, $16.00. Philadelphia: W. B. Saunders Company, 1955.

This excellent book is prepared to introduce the reader to the more important facts about cancer cells. Cancer focusses attention on cells, both normal and malignant, for neither can be appreciated without knowledge of the other.

Twenty clear, concise, well illustrated chapters cover all the phases of normal and cancer cells, analyzing their cyptoplasm, nuclei, and chemical properties. The present day knowledge and the research evidence in the influence of trauma, viruses, mutations, susceptibility, heredity, age, sex, and prevention, are outlined.

As one reads through the voluminous material on cancer cells, one wishes the author had summarized a list of conclusions of practical aid to the general practitioner who is called upon to answer so many questions on cancer in his daily contacts. Such information could relate to vitamins, prevention, nutrition, hormones, heredity, viruses, etc.

However, students of cancer and cytology will find this book extremely helpful. The appendix contains extensive information on cancer research bibliography.

AGING — GENERAL ASPECTS. By G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Margaret P. Cameron, M.A., A.B.L.S., assisted by Joan Etherington. Pp. 255, with 38 illustrations. Cloth. Price, $6.75. Boston: Little, Brown and Company, 1955.

With the span of life advancing toward the century mark, the family physician has fairly well adjusted himself to the consideration of gerontology as one of the most important phases of his daily practice.

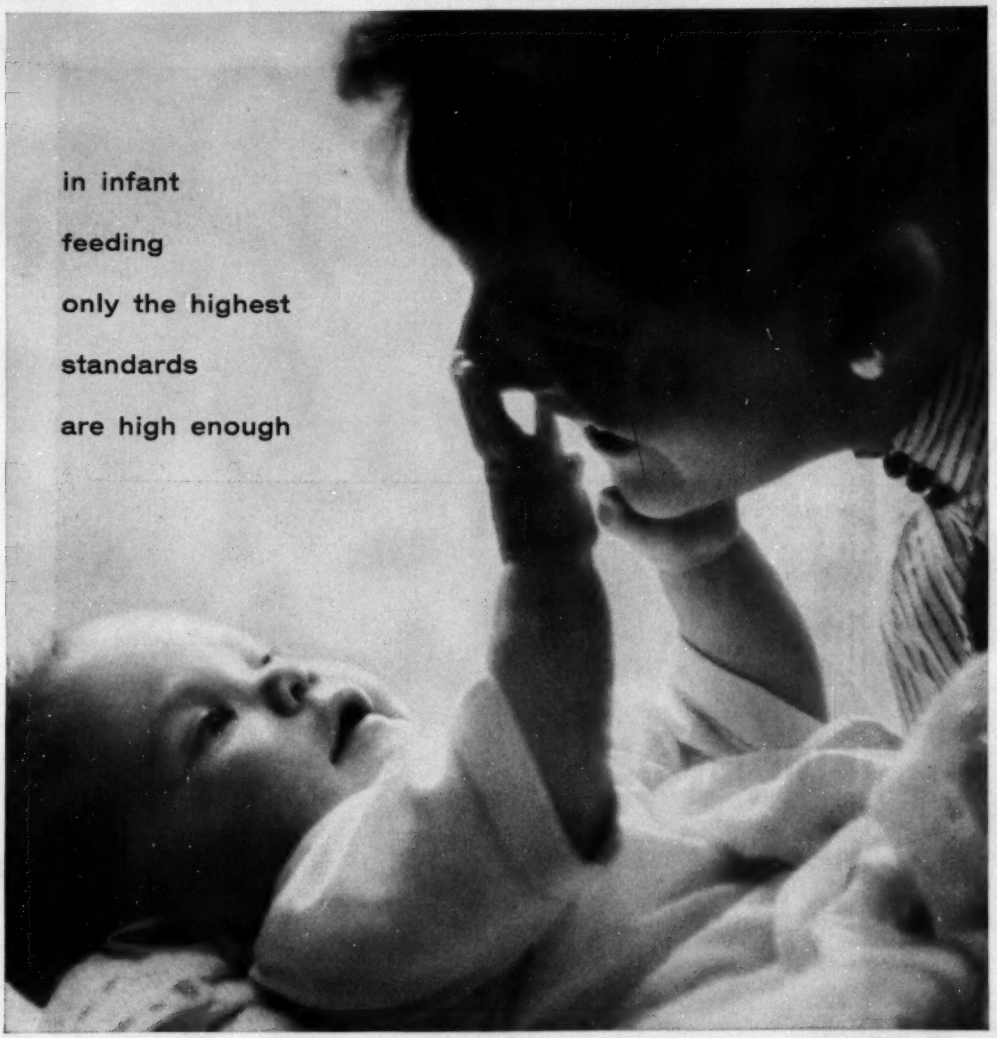
CIBA FOUNDATION COLLOQUIA ON AGING
VOLUME I

This volume, being a concise summary of various aspects of aging, started with the definition and measurement of senescence, the pathological basis and mental aspects, and covering the body systems and their changes with aging. The book ends with a general discussion.

Among many other interesting facts, it was brought out that the response of blood sugar to insulin is uniformly reduced in older individuals. In all instances the rate of disappearance of glucose from the blood of the older groups was substantially less than it was for the young and middle-aged groups. It was also shown that any assessment of aging should be rated to function, and that the functional reserve, or the capacity of the individual under strain, was much more likely to give an indication of aging. Traumatic or environmental and hereditary factors are of vital significance. Genetics in mankind not only influences duration of life, it is stated, but also the form of aging.

Unfortunately, "the expectation that transplants of gonadal tissue would serve to rejuvenate the senescent was illusory".

A general discussion and some references follow each chapter. The book is well indexed.



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